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Pathology

EXPERIMENTAL PATHOLOGY

804. **Transformation of Normal Human Fibroblasts into Histologically Malignant Tissue *in vitro***
L. LEIGHTON, I. KLINE, and H. C. ORR. *Science* [*Science*] 123, 502–503, March 23, 1956. 2 figs., 7 refs.

The transformation of normal human cells into malignant ones was observed in experiments at the National Institutes of Health, Bethesda, Maryland. Fragments of foreskin from a 4-day-old infant were explanted into cellulose sponge matrix in a human-serum–beef-embryo-extract–saline medium. Subcultures were divided into vigorous and less vigorous substrains, the latter being subcultured every 6 to 10 weeks. Except for occasional bizarre forms the outgrowth was consistently of spindle-shaped cells until at 23 months a 15th subculture showed a striking change—large bizarre cells growing gradually at the expense of the spindle-shaped cells. Histologically, the pattern was considered to be typically neoplastic—for example, there were many large, hyperchromatic cells, some with single large nuclei containing enormous nucleoli, and numerous mitoses, many of which were multipolar. Since the cultures were of human origin, no test of malignancy *in vivo* could be carried out. It is considered that a low oxygen tension may have been responsible for the change as suggested by Goldblatt and Cameron, who found that anaerobiosis was a common factor in the production of malignancy *in vitro*. *M. H. Salaman*

805. **Importance of Circulatory Factors in the Pathogenesis of some Subfebrile Conditions.** (Значение циркуляторного фактора в генезе некоторых форм субфебрильного состояния)
P. I. ITSKOV. *Терапевтический Архив* [*Ter. Arkh.*] 28, 59–66, No. 3, 1956. 1 fig., 25 refs.

A detailed comparative study of skin temperatures (measured by determining the heat loss by infra-red radiation from areas of skin) and intragastric temperatures (measured with the thermoelectric apparatus of Savitskii) was carried out on three groups of subjects—healthy afebrile individuals, patients with subfebrile infective disorders, and patients with subfebrile functional disturbances of the cardiovascular or nervous systems, such as transient hypertension and vegetative neuroses.

It was concluded that in non-infective subfebrile states there is a functional disturbance of the central regulator mechanism of the circulation, leading to disordered heat distribution in the organism without disturbance of the heat balance. The stomach temperature in such cases is generally found to be within normal limits (whereas in infective cases it is definitely above normal), while topographical disturbances of the skin temperature are present, with thermo-asymmetry, isothermia, and thermo-inversion. Stomach thermometry may be useful as a differential diagnostic method in prolonged subfebrile states, the gastric temperature being about 0·5° C. higher than that of the skin in the healthy individual and in infective disorders, and the difference being significantly less in cases of neurocirculatory disorders.
R. Crawford

806. **The Reaction of Tissue-culture Cells to Quartz Dust.** (Über die Reaktion von Gewebekulturzellen auf Quarzstaub)
A. LENGEROVÁ, V. J. LENGER, M. ESSLOVÁ, R. TUSCANY, and M. VOLFOVÁ. *Archiv für Gewerbepathologie und Gewerbehygiene* [*Arch. Gewerbepath. Gewerbehyg.*] 14, 311–328, 1956. 11 figs., 6 refs.

The reaction of the intact organism to the inhalation of irritant dusts is a complex process originating from a primary biological effect of the dust particles on the cells of the lung tissue, and two different kinds of dust will produce different reactions in the same organism only if they differ in their primary effects. Although this primary effect of dusts may be studied in tissue cultures of lung cells, the reaction of the intact organism cannot be deduced from the reaction of the isolated cell, which may be modified by other factors, a weak primary effect being augmented or a comparatively strong primary effect depressed. Thus although tissue-culture techniques may be used to determine the biological activity of different dusts, the relation between the primary effect of a dust on the tissue cell and the development of pneumoconiosis remains as an entirely separate problem.

At the Prague Institute of Industrial Hygiene and Medicine experiments were carried out on tissue cultures to determine whether a change in the physical structure of an inert material may result in biological activity.

The cells used were fibroblasts from the heart of a 10- to 12-day-old chick embryo and macrophages from the spleen. The dust used was freshly ground quartz suspended in a 25% dilution of embryonic extract, with and without previous *x*-irradiation for 5 minutes at 40 kV and 12·5 mA. The hanging-drop method of culture was discarded because the tissue reaction is necessarily slow and reinoculation every 72 hours tended

to damage the fragile cells. Instead, a modification of the Carrel flask method was adopted, a fresh suspension of sterilized dust being added once or twice in the 24 hours. To determine whether the cell reaction results from close contact between the tissue cell and the dust particle or from the effect of dust constituents in solution, culture tissue was planted in the Carrel flask at two sites slightly apart, at one of which the tissue was planted upon the surface of a firm clot and at the other within the clot, which would then act as a filter, allowing access of fluid to the tissue cells but preventing passage of solid particles of dust. Control cultures were set up without dust suspension and the effects of irradiated and non-irradiated quartz dust on the cells studied.

The addition of the irradiated dusts had a profound effect upon the development of the fibroblasts, the zone of growth having an irregular margin, the cells varying in form and structure, many being polygonal, some slender, and many vacuolated; in some the nucleus was eccentric, pressed against the cell wall, kidney-shaped, or in a form suggesting that seen in the process of amitotic division. The addition of non-irradiated dust on the other hand had no effect, the cells being practically identical with those of the control cultures. It was shown that very close contact between cell and dust particle is essential for the development of these effects, a thin layer of clot interposed being enough to hinder the reaction. *M. A. Dobbin Crawford*

807. **The Thyroid Gland in Experimentally Induced Neurosis.** (Щитовидная железа при экспериментальном неврозе)

V. I. Arkhipenko. *Проблемы Эндокринологии и Гормонотерапии* [*Probl. Endokr. Gormonoter.*] **2**, 42–50, No. 1, Jan.–Feb., 1956. 6 figs., 6 refs.

In a study of the effect of neurosis on thyroid function, carried out at the Medical Institute, Kharkov, on 8 dogs, a stimulus to defensive reflexes (induction of an electrical shock) was alternated with a stimulus to food reflexes (ringing of a bell) over a period of some days until a condition of neurosis was induced, as shown by behaviour changes, refusal of food, and other emotional signs, the level of thyroid function being measured by noting the rate of uptake of radioactive iodine by the gland before and at intervals after the induction of neurosis.

In 7 out of the 8 dogs there was a distinct fall in this rate, while in some of the animals symptoms of thyroid deficiency, such as loss of hair and trophic skin changes, appeared. During the same period blood from these animals was injected into guinea-pigs and the effect on the thyroid gland examined, whereby the content of thyrotrophic hormone in the dogs' blood could be estimated. In 4 out of 5 dogs showing depression of thyroid function as a result of neurosis the level of thyrotrophic hormone in the blood was not diminished; in fact, in 2 cases it was increased. On the other hand the dog which responded to the induced neurosis by an increase in thyroid function showed a lower serum thyrotrophic hormone level after the experiment than before. This suggests that the fall in thyroid activity in experimental neurosis occurs without any reduction in pituitary thyrotrophic activity and is of direct neurogenic origin.

Treatment of the neurosis by administration of bromide (or, in one case in which this was not effective, by prolonged narcosis) quickly led to a return to a normal uptake of iodine as the neurosis receded. This rapid response to the restoration of higher nervous control is in contrast to the paradoxical response often noted to the thyrotrophic hormone of the pituitary gland.

The mechanism of the phenomenon is discussed at some length, with references to the work of other investigators. The author points out that the condition of the higher centres also directs the character of the response of the thyroid gland to the administration of goitrogens such as 6-methylthiouracil, which in normal dogs leads to an increase in the hypophysial content of thyrotrophic hormone. The same result was obtained in the one dog in this study which reacted to neurosis by an increase in thyroid function; yet the thyroid gland of this animal showed none of the appearances of thyrotrophic stimulation in response to 6-methylthiouracil. On the other hand the responses of the remaining dogs with neurosis to 6-methylthiouracil were conflicting, the pituitary content of the hormone being reduced in one. Thus in all these dogs the relation between the thyrotrophic activity of the hypophysis, the rate of uptake of radioactive iodine, and the reaction of the thyroid gland to the hormone was disturbed, in contrast to dogs with an intact nervous system, in which such parallelism was well marked. *L. Firman-Edwards*

CHEMICAL PATHOLOGY

808. **The Hydration Capacity of the Serum Proteins in Diffuse Diseases of the Liver and Kidney.** (Гидратационные свойства сывороточных протеинов крови больных диффузными заболеваниями печени и почек)

I. V. Dzhavakhishvili. *Терапевтический Архив* [*Ter. Arkh.*] **28**, 16–23, No. 3, 1956. 8 figs.

After a preliminary discussion of the chemistry of protein dispersion and solution in the serum, the method of plotting dehydration curves for the serum proteins is detailed. It is considered that in the molecule of protein —a network of amino-acids joined together by peptide links—there are hydrophil centres of two types: polar lateral chains and atoms of oxygen and nitrogen with peptide linkages. If the amino-acid content of a protein is known it is possible to determine the quantity of water linked to it. Thus in gelatin 2·6 molecules of water are linked to one amino-acid radical.

In certain conditions, such as infective hepatitis, cirrhosis of the liver, and the hepatosplenomegaly syndrome, there is an increase in the stability of the protein in solution in the serum and an increased energy of hydration, the dehydration curve tending to return to normal with improvement in the condition. In diffuse diseases of the kidney on the other hand there is a reduction in the stability of the proteins in solution and in their energy of hydration; when azotaemia is present, how-

ever, the reverse is the case. It is claimed that studies of the hydration capacity of the serum proteins point to the participation of the kidneys in the processes of serum protein exchange and throw some light on the specific interaction of the protein molecule with water.

R. Crawford

809. **Serum Transaminase Activity. Observations in a Large Group of Patients**

M. CHINSKY, G. L. SHMAGRANOFF, and S. SHERRY. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] 47, 108–118, Jan., 1956. 3 figs., 5 refs.

The enzyme glutamic oxalacetic transaminase is normally present in the blood and, in high concentration, in such tissues as heart, liver, kidney, muscle, and brain. Serum transaminase activity, which has been reported to be significantly increased in conditions associated with myocardial or hepatic necrosis, was assayed by Karmen's method in 15 healthy young adults and in 400 patients with various diseases at the Jewish Hospital of St Louis (Washington University School of Medicine) in an attempt to assess the diagnostic value of its determination. The results of 50 assays on specimens of serum from the 15 normal subjects ranged from 7 to 40 units per ml. (average 20 ± 8 units per ml.), those of duplicate estimations agreeing within 10 units per ml., and the upper limit of normal was therefore arbitrarily taken as 50 units per ml., values between 41 and 50 units being regarded as doubtful. The occurrence of a high serum transaminase activity was associated with the appearance of significant amounts of the enzyme in the urine, but the level of activity was very low compared with that in serum. Bile obtained at operation in 2 cases, however, contained large amounts of transaminase.

Of 117 patients with myocardial infarction, 108 (92%) had abnormally high levels of serum transaminase activity. Serial estimations showed a definite increase in the level starting approximately 6 hours after the onset of the attack, rising to a peak at about 24 hours and falling again to within the normal range by the 3rd to the 6th day. A very high serum transaminase level was usually associated with a poor prognosis, 13 of 25 patients (52%) in whom the level was above 200 units per ml. dying compared with 14 out of 85 (16%) in whom the level was below 200 units per ml. In none of 69 patients with angina pectoris but without evidence of infarction was the level raised. High levels were also found in 8 out of 15 cases of cardiac arrhythmia, being present only when the heart rate was above 160 per minute, in 14 out of 15 cases of hepatitis, in 7 out of 9 cases of hepatic cirrhosis with jaundice, in 8 out of 10 cases of obstructive jaundice, in each of 5 cases of secondary carcinoma of the liver, and in 8 out of 10 cases of acute pancreatitis with jaundice and in 3 out of 6 without jaundice. Normal levels were found almost invariably in cases of acute pulmonary oedema, chronic congestive failure, benign pericarditis, cerebral vascular accident, and various other diseases, including 4 cases of chronic uraemia and one of acute anuria.

It would therefore appear that increased transaminase activity in the serum is associated in particular with necrosis of heart muscle and liver tissue, with jaundice of any type, and with very rapid cardiac arrhythmia, and that it does not result from deficient urinary excretion. The amount of transaminase liberated into the blood stream is probably determined by the amount of tissue involved in the necrotic process and by the transaminase content of that tissue. It is therefore likely that necrosis of any tissue containing the enzyme, if sufficiently extensive, will result in an increase in the serum transaminase level, but that it is only in the heart and the liver that this commonly occurs.

In the authors' opinion the assay of serum transaminase activity is of most value, in the present state of knowledge, in excluding the presence of significant myocardial or hepatic necrosis. *Robert de Mowbray*

HAEMATOLOGY

810. **Delayed Prothrombin Estimation in Outpatient Anticoagulant Therapy**

H. WATSON. *Lancet* [*Lancet*] 1, 541–543, April 28, 1956. 1 ref.

The object of this investigation, which was carried out at the Royal Infirmary, Edinburgh, was to determine whether freshly-drawn specimens of blood—that is, blood withdrawn not more than 30 minutes before—were essential for satisfactory estimation of the prothrombin time in out-patients undergoing prolonged anticoagulant therapy. Specimens of blood were collected in 1·34% sodium oxalate solution and the prothrombin time was estimated by the one-stage method immediately and 24 hours after withdrawal. It was found that the prothrombin time of specimens sent through the post and thus tested 24 hours after collection was similar to that of fresh blood, and could be utilized to maintain satisfactory anticoagulant therapy. Moreover, the use of plasma instead of whole blood did not appear to influence the results. In further experiments it was found that the prothrombin time of specimens sent by post was again similar to that of specimens stored for the same period in a refrigerator. Haemolysis by mechanical means did not have any significant effect on the prothrombin time, but when haemolysis was due to contamination with surgical spirit the results were fallacious. *A. S. Douglas*

811. **Origin of Leukemic Cells in Monocytic Leukemia**

M. N. RICHTER. *Laboratory Investigation* [*Lab. Invest.*] 5, 155–161, March–April, 1956. 3 figs., 10 refs.

Histological material from 45 cases of monocytic leukaemia was examined at the New York University–Bellevue Medical Center, New York, to determine the part played by the reticulo-endothelial system in this disease. The blood picture in these cases corresponded with that described by others, the total leucocyte count ranging from 250 to 560,000 cells per c.mm. of blood. Nuclear convolution was a conspicuous feature. Leukaemic cells were present in the sinuses and pulp of the spleen and lymph nodes, the sinuses and portal spaces of the liver, and the interstitial tissue of various organs Amoeboid activity was noted in a number of cases, cells

being seen, for instance, in transit through the walls of the splenic sinuses. Hypertrophy of reticulum cells of the splenic sinuses, lymph nodes, and other tissues was not uncommon, and many of the free mononuclear cells in the sinuses may have arisen therefrom, but they were of the phagocytic type and bore neither resemblance nor relationship to the leukaemic cells present.

There was no evidence that leukaemic cells originated from endothelial tissue other than bone marrow. The condition in these cases appeared to correspond to the so-called Naegeli type of monocytic leukaemia and was regarded as myelogenous, inasmuch as the cells apparently arose from primitive elements in the bone marrow.

Mary D. Smith

812. **The Platelet-like Activity of Certain Brain Extracts**
J. V. GARRETT. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **47**, 752–759, May, 1956. 3 figs., 20 refs.

813. **Haematopoiesis in Cancer.** (Кроветворение при раковой болезни)
A. A. BAGDASAROV, M. S. DULZHTSIN, M. Y. ANSHEVITS, and R. I. RODINA. *Терапевтический Архив* [*Ter. Arkh.*] **28**, 3–11, No. 3, 1956. 3 figs., 11 refs.

Previous work by the authors at the State Medical Institute, Moscow, has shown that in the early stages of the development of cancer of the stomach the bone marrow shows certain definite and constant changes—megakaryocytes with multiple fragmentation of the nucleus and a basophil cytoplasm containing large numbers of blood platelets, mononuclear megakaryocytes, a lowered erythroblastic maturity coefficient, and a reduction in the number of promyelocytes and an increase in that of mature neutrophil granulocytes present. To determine whether these changes were of diagnostic significance their investigation was extended to cases of other gastric conditions, mainly peptic ulcer (17) and polyposis (17), and to cases of cancer of the lung (26).

In cases of cancer of the lung the bone marrow generally showed no very definite changes. The same type of abnormality was seen in the megakaryocytes and the erythrocyte:normoblast index was reduced, but less frequently than in cancer of the stomach. The number of mature neutrophil cells present was increased and plasma-cell reactions were observed fairly often. In the peripheral blood there was generally a moderate thrombocytosis, but only in the presence of metastases or haemorrhage was this considerable in degree. In ulcerative conditions of the stomach a change in the leucoblast:erythroblast ratio occurred with considerable frequency. The peripheral blood showed a slight macrocytosis and, after haemorrhage, a moderate and transient thrombocytosis. In polyposis of the stomach no significant changes in the bone marrow or peripheral blood were observed. Hence the appearance, in cases of peptic ulcer or polyposis of the stomach, of bone-marrow changes characteristic of cancer of the stomach suggests that malignant degeneration has occurred.

R. Crawford

MORBID ANATOMY AND CYTOLOGY

814. **The Pathological Anatomy and Pathogenesis of Concussion.** (К патологической анатомии и патогенезу сотрясения головного мозга)
B. I. SHARAPOV. *Вопросы Нейрохирургии* [*Vop. Nejrokhir.*] 8–11, No. 2, March–April, 1956. 2 figs.

A morphological study of the brain in 9 fatal cases of concussion is presented. The author found evidence of rupture of pre-capillary arterioles in the tectum of the midbrain at the level of the corpora quadrigemina. This could have been produced by sudden displacement of the brain. Another change found in several parts of the brain was oedema of nerve cells and their nuclei, with irregularity of outline in the capillaries adjoining these cells and in the end-organs and fibrils of the pericellular apparatus.

L. Crome

815. **The Physiology of Human Cartilage.** (К физиологии хрящевой ткани человека)
T. P. VINOGRADOVA. *Архив Патологии* [*Arkh. Patol.*] **18**, 24–30, No. 2, 1956. 7 figs., 19 refs.

In this description of a histological study of normal and dystrophic human cartilage carried out at the Institute of Traumatology and Orthopaedics, Moscow, the author reports that cartilage grows in a twofold manner: (1) by apposition, and (2) by increase of interstitial tissue. Growth by apposition implies transformation of the perichondrium and other contiguous tissue into cartilage. In regard to interstitial growth the author observes that even the most differentiated cells in the cartilage do not lose their proliferative ab ility In certain forms of dystrophy a chondro-mucoid substance can be seen to penetrate into the surrounding tissue and veins. It is pointed out that "asbestization" of the matrix is not a mere unmasking of pre-existing collagen fibres, but involves the new formation of such fibres.

L. Crome

816. **Macrofollicular Lymphoma**
C. J. E. WRIGHT. *American Journal of Pathology* [*Amer. J. Path.*] **32**, 201–233, March–April, 1956. 15 figs., 34 refs.

The author reports 136 cases of macrofollicular lymphoma studied at the Harvard Cancer Commission's laboratories, Boston, with special reference to the relation between this condition and other lymphoid disorders and its existence as a separate pathological entity. The histological characteristics of macrofollicular lymphoma are described in detail and its differentiation from lymphoid hyperplasia, and especially giant follicular hyperplasia, discussed. Several cases were available in which the histological structure of nodes obtained at biopsy could be compared with subsequent biopsy findings or with the eventual necropsy findings, and the relationship between the appearances at different stages is commented on and the existence of the disease as an entity established.

It is argued that the natural and characteristic progression of macrofollicular lymphoma is into diffuse

lymphoma, but as this development may occur at any time "it is impossible to attach individual prognostic connotation to the disease and only generalizations can be made". In fact, the over-all prognosis as judged from the present series of cases is not so good as previous reports would suggest, the 5-year survival rate being 36·1%. However, where localized disease only is present the prognosis may be good. *J. B. Wilson*

817. **A Histochemical Study of Pulmonary Hyaline Membrane**

F. Duran-Jorda, A. Holzel, and W. H. Patterson. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 113–118, April, 1956. 12 figs., 10 refs.

At Booth Hall Children's Hospital, Manchester, a series of laboratory investigations were carried out to determine the nature of the pulmonary hyaline membrane. All the material examined showed peroxidase activity—that is, a positive reaction to the Pickworth stain—and its absorption of violet and of ultraviolet light was somewhat similar to that of blood. After micro-incineration of the material some iron-containing ash was left. In the authors' view the results suggest that the membrane is a blood product of endogenous origin. Paraffin sections were made of the residue obtained by dialysing amniotic fluid against 10% dextran. No eosinophil hyaline material was seen, indicating, it is suggested, that hyaline membrane is not derived from amniotic fluid. [It would have been of interest if the same histochemical and histophysical methods had been applied to the amniotic residue.] *M. C. Berenbaum*

818. **Infantile Lobar Emphysema. An Etiological Concept**

R. B. Bolande, A. F. Schneider, and J. D. Boggs. *A.M.A. Archives of Pathology* [*A.M.A. Arch. Path.*] **61**, 289–294, April, 1956. 15 refs.

In recent years a form of emphysema in young infants distinct from the obstructive and compensatory types has been recognized, and has been variously described as congenital emphysema, hypertrophic emphysema of infants, and infantile lobar emphysema. Clinically, this disorder is often confused with congenital cystic lung, both commonly causing the sudden onset of respiratory distress and cyanosis. In congenital cystic lung this is due to valvular obstruction by bronchial exudate of the communication—usually very narrow—between cyst and bronchial tree, resulting in a rapid expansion of the cyst, but no such obstruction is found in the majority of cases of infantile lobar emphysema.

In the records of the Children's Memorial Hospital, Chicago, for the period 1938–54 the authors found 7 cases in which the following criteria were satisfied: (1) onset of respiratory distress in the neonatal period; (2) surgical (6 cases) or necropsy (one case) evidence of localized pulmonary emphysema, which was primary and more severe in degree than other changes in the lungs; (3) absence of other diseases of the heart and respiratory system. Specimens of lung tissue from these cases, from 2 cases of emphysema of other types, and from 6 cases of non-respiratory disease were studied and compared, and 23 cases of infantile lobar emphysema reported in the literature were reviewed. In 5 of these last and in 2 of the authors' own cases there was hypoplasia of the bronchial cartilages (chondromalacia) and in 8 out of the total of 30 cases there was an intrinsic or extrinsic bronchial stenosis, but the majority of cases showed no bronchial abnormality. A constant finding in the authors' cases was a thickening of the alveolar septa containing elongated cells in a matrix of delicate, slightly refractile fibrils, both cells and fibrils staining bright blue with Mallory's aniline blue. This material was thought to represent an abnormal deposit of immature collagenous connective tissue, and it is suggested that such a "fibrous dysplasia", congenital in origin, may be an important aetiological factor in infantile lobar emphysema. The relation between this condition and the congenital alveolar dysplasia described by MacMahon (*Amer. J. Path.*, 1948, **24**, 919; *Abstracts of World Medicine*, 1949, **5**, 557) is discussed, the former possibly resulting from rapid differentiation of the mesenchymal tissue present in the alveoli in an infant with the latter condition who survives. *H. S. Baar*

819. **Changes at Different Levels of the Nervous System and in the Lungs in Bronchial Asthma.** (Изменения в различных отделах нервной системы и в легких при бронхиальной астме)

I. M. Kodolova. *Архив Патологии* [*Arkh. Patol.*] **18**, 73–82, No. 2, 1956. 6 figs., 17 refs.

In the post-mortem histological study of 4 fatal cases of bronchial asthma here reported from the Order of Lenin Medical Institute, Moscow, the author found non-specific changes in nerve morphology, these being particularly marked in the ganglion nodosum, in the fibres of the vagus, and in its dorsal medullary nucleus. The changes in the sympathetic nervous system were less conspicuous. In the lungs the nerves most affected were those of large and medium calibre. The author suggests that the degree and character of the changes depend on the functional activity of the different parts of the nervous system and also on their oxygen requirement. Thus since the more active elements require a greater amount of oxygen, they suffer more severely from the anoxia which results from asthmatic attacks. *L. Crome*

820. **Arteriosclerosis in the Intramural and Extramural Portions of Coronary Arteries in the Human Heart**

J. C. Edwards, C. Burnsides, R. L. Swarm, and A. I. Lansing. *Circulation* [*Circulation (N.Y.)*] **13**, 235–241, Feb., 1956. 4 figs., 1 ref.

In a study of 276 human hearts to determine the incidence of intramural coronary arteries, with all or a major portion of coronary artery covered entirely by myocardium, we found 15 such intramural arteries; an incidence of approximately 1 intramural coronary artery among every 23 examined. One additional heart with an intramural coronary artery was found but was not in the consecutive group of autopsies. In no instance was there more than one coronary artery intramural in any heart. All but two of the intramural coronary arteries

exhibited severe atheromata and narrowing of the lumina. The other extramural coronary arteries in these hearts showed atherosclerotic involvement also. Eight of the intramural coronary arteries had marked atherosclerosis, 6 had moderate and 2 had slight atherosclerosis.

From the above findings one may assume that the covering of a coronary artery in the human heart by myocardium during a part of its major course fails to protect it from the atherosclerotic process which occurs there in much the same type and incidence as it does in the extramural portions of the same arteries and in other entirely extramural coronary arteries.—[Authors' summary.]

821. **The Significance of Adventitial Infiltrations in Coronary Atherosclerosis**
L. M. GERLIS. *British Heart Journal* [*Brit. Heart J.*] **18**, 166–172, April, 1956. 2 figs., 19 refs.

The author has attempted to correlate the histological findings in the coronary arteries with the cause of death in patients dying of coronary arterial disease, basing his conclusions on the results of 160 necropsies performed at Grimsby General Hospital, of which 101 were on patients dying from this disease, while in 59 control cases death was due to some other cause.

Adventitial lesions, consisting of aggregations of small round cells around the vasa vasorum of the large coronary arteries, were seen in 80% of the 101 coronary cases, but were present in only 17 (29%) of the 59 control cases. Of those coronary cases in which there had been sudden death without infarction (47 cases), adventitial lesions were present in 44, that is, over 90%. Of the 34 cases in which an old infarction or myocardial fibrosis was found at necropsy, 25 (74%) showed adventitial lesions, while of the 20 cases in which there had been recent infarction the lesions were present in 13 (65%). There was no significant relationship between the degree of coronary atheroma and incidence of adventitial infiltrations; the latter appeared to be related more closely to the cause of death. In all of the 17 control cases with adventitial infiltrations the cause of death had included an associated anoxic element. It is therefore suggested that in the coronary cases local anoxia resulting from spasm of the vessels, particularly the small vessels of the coronary adventitia, is the cause of the adventitial infiltrations. The author also suggests that these infiltrations are related to the terminal mechanism responsible for death, since they do not show any evidence of organization or fibrosis, even when quite large. *R. B. Lucas*

822. **The Pathogenesis of Valvular Thickening in Rheumatic Heart Disease**
P. S. TWEEDY. *British Heart Journal* [*Brit. Heart J.*] **18**, 173–185, April, 1956. 12 figs., 27 refs.

In a study of the pathogenesis of valvular thickening in rheumatic heart disease the cardiac valves of 29 patients dying from this condition were examined at the Royal Victoria Infirmary, Newcastle upon Tyne. Examination for surface deposits showed that these occurred most often in the commissures between thickened cusps on the contact line of the valve and on the extreme tip; they were less commonly found on the chordae tendineae and elsewhere. Vegetations were shown to consist of acidophil material which stained partly for fibrin and partly not. A study of the changes immediately preceeding the formation of vegetations revealed that neither fibrinoid change nor underlying inflammation was necessarily present at the onset of thrombus deposition, though some damage to the endothelium appeared to be a necessary precondition.

Thrombus deposits were found on valves at all stages of the disease, and these are considered to be responsible for much of the thickening in rheumatic valvular disease. They also appeared to be the cause of the fusion of chordae to each other and to valve cusps, as well as of the incorporation of chordae tendineae into valve cusps. The thrombus deposits were found to consist of fibrin and probably also platelets. Since they were very widespread it is suggested that most of the actively proliferating tissue in the valves in acute valvulitis may be due to the organization of successive thin deposits rather than to a primary proliferation. *R. B. Lucas*

823. **Periarteritis Nodosa. Its Relationship to Endomyocardial Sclerosis**
J. WATT and J. B. LYNCH. *Lancet* [*Lancet*] **1**, 658–660, May 12, 1956. 5 figs., 21 refs.

The authors report from Liverpool University the case of a boy aged 12 who, in March, 1955, was admitted to hospital with a pyrexial illness which was thought to be due to a perinephric abscess and which responded favourably to treatment with penicillin and streptomycin. Four months later, however, he died suddenly during the night, a few hours after complaining of mid-abdominal pain. Necropsy revealed endomyocardial sclerosis of the left ventricle, thrombosis of the splenic and the superior mesenteric arteries, old infarctions of the spleen, and early peritonitis. Typical lesions of acute periarteritis nodosa were found in the superior mesenteric artery, the aortic vasa vasorum, and the vessels of the pancreas and testes. The literature relating to the association between endomyocardial sclerosis and periarteritis nodosa is reviewed, with particular reference to Loeffler's " endocarditis parietalis fibroplastica ".
L. Crome

824. **Occlusive Arteries and Arterio-venous Anastomoses in Myocardial Infarcts.** (Замыкающие артерии и артерио-венозные анастомозы при инфарктах миокарда)
P. O. UL'YANETSKAYA. *Архив Патологии* [*Arkh. Patol.*] **18**, 44–52, No. 2, 1956. 7 figs., 16 refs.

In this histological study of occlusive arterioles and arterio-venous anastomoses in the muscle and scar tissue of myocardial infarcts the author traces the evolution of these structures, and describes the development of smooth muscle fibres in the occlusive arterioles from poorly differentiated vascular connective tissue and, secondly, the proliferation of the endothelial and perivascular tissue elements and their subsequent conversion into muscle. *L. Crome*

Microbiology and Parasitology

825. **Mixed Staphylococcal Infections. The Development of Penicillin-resistant Strains**
R. W. FAIRBROTHER. *Lancet* [*Lancet*] **1**, 716–719, May 19, 1956. 10 refs.

In an investigation at Manchester Royal Infirmary the author found, in common with other workers, that the majority of strains of *Staphylococcus aureus* isolated from infective processes at the present time are resistant to penicillin. Careful examination of the colonies in the primary cultures showed that, in some, two varieties could be distinguished. In 12 instances the organisms from one of the colonies produced penicillinase, whereas those from the other colony were unable to do so. In 5 the phage pattern of the two colonies was identical, in 4 it was different, and in 3 the phage pattern of one of the two varieties could not be determined.

Further experiments showed that from 10 out of 14 apparently pure strains, which were resistant to penicillin because they produced penicillinase, penicillin-sensitive variants could be obtained by subcultivation in broth at 44° C. Of these 10, 8 were then subcultured 20 times on agar plates at 33° C. and from 2 of them penicillinase-producing variants were isolated. On the other hand no penicillinase-producing variants were detected as a result of similar treatment of another 8 strains sensitive to penicillin, but recently isolated from infective processes.

The author advances the theory that the original wild strain of *Staph. aureus* was probably able to produce penicillinase, but that with increasing adaptation to the human nares the majority of strains have lost this function. With the widespread use of penicillin as a therapeutic agent, many penicillin-sensitive strains have been eliminated, their places being taken by descendants of the few penicillinase-producing strains which had survived as human parasites. *R. Hare*

826. **Varied Degrees of Isoniazid Resistance within Strains of Tubercle Bacilli from Sputum and Pulmonary Cavities**
S. M. STEWART. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **73**, 390–405, March, 1956. 5 figs., 12 refs.

In this paper from the University of Edinburgh the results are reported of an investigation into the degree of isoniazid resistance found in strains of tubercle bacilli isolated from three groups of patients: (1) 8 patients who had never received the drug; (2) 7 who had been treated with isoniazid for varying periods of time and whose organisms were known to be resistant; and (3) 2 patients in whom the organisms, having become resistant during previous treatment, had become less resistant after treatment had ceased, and who were being given a course of isoniazid for the second time. A series of fourfold dilutions of isoniazid in distilled water were added to plates of Löwenstein–Jensen medium to give final drug concentrations of 0·06 to 64 μg. of isoniazid per ml. These were inoculated with 0·02 ml. of a series of tenfold dilutions of a homogenate of the patient's sputum prepared after digestion with 4% sodium hydroxide; viable counts were also carried out on plain Löwenstein–Jensen medium. The plates were then incubated for 8 weeks at 37° C.

The organisms from all the patients in Group 1, with one exception, were uniformly sensitive, while in the remaining instance 4 colonies grew from undiluted sputum concentrate in the presence of 0·06 μg. of isoniazid per ml., that is, only one organism in every 4,000 was resistant to this concentration of the drug. In Group 2, in 5 of the 7 cases there was great variability in the proportion of organisms which proved to be resistant to a given concentration of isoniazid. In only one case were all the organisms resistant to the highest concentration which permitted growth to occur. For the 2 patients in Group 3 weekly studies of the distribution and percentage of isoniazid-resistant strains were carried out, the detailed results of which are presented in tables.

The author also carried out an examination of organisms recovered from lung cavities; this showed that although the distribution of resistance was more uniform, in no case were all of the organisms resistant to the highest concentration of isoniazid at which growth occurred. *John M. Talbot*

827. **Studies on the Distribution of Drug-resistant Tubercle Bacilli within the Lung**
F. W. A. TURNBULL and S. M. STEWART. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **73**, 406–421, March, 1956. 1 fig., 16 refs.

In this further study from the University of Edinburgh [see Abstract 826] an investigation was made of the isoniazid resistance of tubercle bacilli obtained from cavities and caseous foci in 13 patients with advanced tuberculosis, all of whom had been treated with varying dosages of isoniazid, streptomycin, and PAS for long periods; investigation of streptomycin resistance was also undertaken in 8 of the cases. In both studies the methods of investigating resistance, which are briefly described, were those recommended by the Medical Research Council.

There was considerable variation in the degree of resistance to isoniazid found in 4 out of 13 cases and to streptomycin in 6 out of the 8 cases examined. There was no evidence that the nature of the lesion from which the organism was obtained had any effect on the degree of resistance found; organisms from 2 of the 4 cases which yielded bacilli of varying resistance to isoniazid were examined for streptomycin resistance, and in neither case was the maximum degree of resistance to both drugs found only in cultures from the same lesion. *John M. Talbot*

828. **Clinical Investigations on Attenuated Strains of Poliomyelitis Virus**

H. KOPROWSKI, T. W. NORTON, G. A. JERVIS, T. L. NELSON, D. L. CHADWICK, D. J. NELSEN, and K. F. MEYER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 954–966, March 17, 1956. 10 figs., 19 refs.

In previous trials living attenuated poliomyelitis virus of the SM (Type 1) and TN (Type 2) strains were administered by mouth to 155 persons, mostly children, with safety and stimulated the production of type-specific antibodies. Further trials are now reported in which the minimum effective dose of these strains, the degree of contagiousness, and the effect of gamma globulin on the establishment of alimentary infection were investigated (with the assent of the parents) in 70 mentally defective children. Information was also obtained concerning the " interference " of the two strains, the effect of certain drugs on faecal excretion of the virus, and the antibody response of previously immunized persons to a second dose.

The SM virus is a rodent-adapted strain of Type-1 poliomyelitis virus, capable of growing in chick-embryo tissue culture, which will occasionally produce paralysis on intraspinal injection in monkeys, but which is non-pathogenic on intracerebral inoculation. Two hard gelatin capsules, each containing 0·5 ml. of recently thawed virus material, were swallowed by each child, together with 8 ml. of milk. Antibodies were produced and alimentary infection was established in 2 out of 3 subjects when the dose ingested was only 2 plaque-forming particles (P.F.P.) of virus; with 20 P.F.P. infection and serological response occurred in 4 out of 4 persons. To test the contagiousness of this strain of virus 5 physically and mentally disabled children who were excreting the virus in the faeces were placed for 3 hours daily for 20 days on a plastic " play mat " with 7 similar children who had not received the virus and whose blood contained no antibodies against it: 3 children in the latter group became infected. In another experiment 12 children who were excreting virus and 7 who had not been fed virus and were susceptible were placed together in an open ward, an attempt being made to prevent direct contact between them. Two of the latter became infected and in both instances contact with an infected child had been observed.

The TN virus is a rodent-adapted strain of Type-2 poliomyelitis virus which is non-cytopathogenic for tissue cultures, its presence being demonstrated by intraspinal infection in albino mice. It was administered in liquid form. As the excretion of this strain occurred only sporadically and in low concentration the development of antibodies was used as the criterion of infection. Although one individual developed antibodies after receiving 300 mouse paralytic doses, 2 out of 3 subjects failed to show a serological response when given a dose 10 times larger. Past experience having shown that the TN strain was not contagious, this was not further investigated.

No significant suppression of the faecal excretion of the Type-1 virus was shown when calomel, albumin tannate, or diiodohydroxyquin was given by mouth, although calomel had a slight effect. The simultaneous administration of both strains of virus resulted in one strain establishing itself to the exclusion of the other, though this interference could be minimized by giving the two strains separately at an interval of 72 days. The development of antibody as a result of oral vaccination was not affected by the simultaneous injection of gamma globulin, nor did the latter affect the development of the intestinal carrier state. Of 19 subjects who had been given the Type-2 virus 3 years previously and who had developed antibodies, a further dose of the original material, which had been stored frozen in the interval, had a " booster " effect on the antibody level in 16, and 10 again became faecal excreters of the virus.

[It is impossible to summarize adequately the wealth of clinical, laboratory, and epidemiological information which this paper contributes to the study of live poliomyelitis vaccines.] *J. E. M. Whitehead*

829. **The Biological Diagnosis of Mumps.** (Le diagnostic biologique des oreillons)

R. A. MARQUÉZY, C. BACH, and J. ACAR. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **32**, 1127–1131, March 30, 1956. 2 figs., 15 refs.

In 22 cases of mumps studied at the Hôpital Trousseau, Paris, 5 of which presented with signs of meningitis only, the value of laboratory methods of diagnosis was assessed. The authors estimated the serum amylase level in 19 cases, and performed Hirst's haemagglutination-inhibition reaction in 17 and the complement-fixation test in 21. The patients' ages varied between 10 months and 9 years.

In 6 healthy children of comparable age the serum amylase level was always below 80 units per 100 ml., whereas in all but 2 of the patients with mumps it rose above 100 units per 100 ml. at some time during the first 15 days, in one case reaching 533 units per 100 ml., although the time of occurrence of the rise was very variable and unrelated to the clinical course. The serum amylase level was estimated once only, on the 5th and 7th days respectively, in 2 cases of meningitis without definite enlargement of the salivary glands and was 160 units per 100 ml. in both. The authors recommend that the haemagglutination-inhibition reaction be performed at the beginning of the illness and again 2 weeks later, a rise in titre being constantly found during this period in their own cases. The complement-fixation test with the V antigen did not give positive results before the 10th day of the illness, and in one case the reaction was still negative on the 18th day. No definite positive reaction was obtained in 7 out of 21 cases, but in 4 of these the test was carried out before the 10th day.

The authors consider that these three tests, which should be regarded as complementary to each other, are of value in the diagnosis of doubtful cases of mumps, particularly those with meningeal manifestations only. In the present series they were able to diagnose mumps in 2 cases in which the only clinical evidence was a rise in temperature at the appropriate interval after exposure to the disease. *Franz Heimann*

Pharmacology

830. Evaluation of Drugs for Protection against Motion Sickness Aboard Transport Ships

U.S. Army, Navy, Air Force Motion Sickness Team. *Journal of the American Medical Association* [*J. Amer. Med. Ass.*] **160**, 755–760, March 3, 1956. 8 refs.

This paper reports the results of a carefully controlled trial of the value of 26 different compounds in combating sea-sickness which was carried out between November, 1954, and April, 1955, on 16,920 members of the U.S. Armed Forces aboard troop transport ships.

Of these, the three best were found to be cyclizine ("marezine") 50 mg. thrice daily, meclizine ("bonamine") 50 mg. once or thrice daily, and promethazine ("phenergan") 25 mg. thrice daily, all of which protected 65 to 70% of subjects. Of the three, meclizine showed the greatest duration of action, and was equally effective whether given twice or thrice daily. The incidence of side-effects was low with all three drugs, though promethazine produced significant drowsiness. Hyoscine produced very severe side-effects on repeated administration, so that it is recommended only for short exposures. Chlorpromazine was ineffective and so were the reserpine alkaloids. *Ronald Woolmer*

831. Site and Mode of Action in the Central Nervous System of Some Drugs Used in the Treatment of Parkinsonism. [In English]

E. W. J. De Maar. *Archives internationales de pharmacodynamie et de thérapie* [*Arch. int. Pharmacodyn.*] **105**, 349–365, March 1, 1956. 4 figs., 45 refs.

In this paper from the University of Utrecht the author describes experiments on cats involving the production of Parkinsonian-like lesions in these animals, the object being to investigate the possibility of the symptomatic treatment of Parkinsonism with cholinergic ganglion-blocking agents. He found that scopolamine, atropine, and L-hyoscyamine given intravenously in doses of 0·5 to 2 mg. per kg. body weight depressed the ipsilateral flexor reflex of thalamic cats, that is, cats in which the cerebral hemispheres and most of the basal ganglia had been extirpated. Similar doses of the same drugs in decerebrate cats had only a very slight effect, if any. He next resected parts of the diencephalon of thalamic cats at various levels. This showed that large parts of the optic thalami and hypothalamus could be removed without altering the depressor effect of scopolamine upon the spinal reflex, but when the ventro-caudal diencephalon was damaged scopolamine no longer depressed the flexor reflex; however, section below the ventro-caudal region caused an increase in reflex intensity. In order to eliminate any direct effect on the spinal cord, scopolamine in one-tenth of the systemic dose was then injected into the vertebral artery of thalamic cats, but still depressed the flexor reflex. Similar depressor effects were obtained with atropine, L-hyoscyamine, diethazine, and "disipal". Caramiphen hydrochloride caused the same depressor effects in decerebrate cats as in thalamic cats. Electrical stimulation of the ventro-caudal diencephalon and the adjoining structures resulted in facilitation and inhibition of the ipsilateral flexor reflex, stimulatory points for inhibitory effects showing a preference for the ventro-caudal part of the diencephalon. When an inhibitory effect was obtained, scopolamine depressed this effect, but there was no corresponding depression of facilitatory effects. The author postulates that the depressant action of scopolamine upon the flexor reflex under the influence of the intact ventro-caudal diencephalon may explain the relief of rigidity obtained with the drug in Parkinsonism, while the action upon the inhibitory centres in the brain stem would explain the lessening of the tremor. *I. Ansell*

832. The Action of Ethyl Alcohol on Gastric Acid Secretion

B. I. Hirschowitz, H. M. Pollard, S. W. Hartwell, and J. London. *Gastroenterology* [*Gastroenterology*] **30**, 244–256, Feb., 1956. 6 figs., 9 refs.

For the purpose of investigating the stimulatory action of alcohol on gastric secretion, which though well known is not well understood, ethyl alcohol in concentrations ranging from 4 to 16% was administered intravenously to 18 healthy male adults and the subsequent gastric output of free hydrochloric acid determined. The response was found to be roughly proportional to the amount of alcohol given. The administration of 1 mg. of atropine subcutaneously before or after the injection of alcohol reduced or even suppressed the response. The same amount of atropine administered during continuous intravenous histamine administration reduced the volume of secretion without, however, affecting the acid concentration.

In an attempt to determine whether the site of action of the alcohol was proximal or distal to the vagal ganglia 12·5 to 25 mg. of hexamethonium bromide was then given subcutaneously; this suppressed basal secretion, but did not prevent the secretory response to a subsequent injection of alcohol from reaching the control level. (The effect of hexamethonium given after the injection of alcohol was not investigated.) The same amount of hexamethonium also failed to block the response to a subsequent intravenous injection of 8 units of insulin. To confirm that the action of alcohol was indeed central it was shown that vagotomy performed on a dog during the intravenous injection of ethyl alcohol abolished the response, while as further confirmation no response was obtained to either alcohol or insulin hypoglycaemia in a patient in whom a vagotomy had been performed previously. From these findings the authors conclude that the gastric secretory response to the systemic administration of alcohol is due to stimulation of the vagal nuclei in the medulla similar to that produced by insulin hypoglycaemia. *R. Schneider*

Chemotherapy

833. **Local Lipodystrophy from Repeated Injections of Streptomycin.** (Lipodistrofia locale da iniezioni ripetute di streptomicina)

M. MIDULLA. *Rivista della tubercolosi e delle malattie dell'apparato respiratorio* [*Riv. Tuberc.*] 3, 562–576, Nov.–Dec., 1955 [received April, 1956]. 8 figs., 20 refs.

The author describes 7 cases (out of 350) in which permanent local lipodystrophy occurred as a result of repeated injections of dihydrostreptomycin into the same area. The patients were children suffering from tuberculous meningitis, and were treated at the Paediatric Clinic of the University of Rome, 4 injections being given daily for 339 to 667 days, always in the region of the buttocks. The lesions [which are very clearly illustrated in the photographs reproduced] were bilateral in 6 cases. The condition is considered to be principally due to a local toxic effect, the mechanism being similar to that of insulin lipodystrophy. However, the possibility of a disturbance of pituitary function as a contributory factor was suggested by the occurrence of a generalized adiposis in 5 of the cases. *Arnold Pines*

834. **Effect of Nystatin on Growth of *Candida albicans* during Antibiotic Therapy**

A. J. CHILDS. *British Medical Journal* [*Brit. med. J.*] 1, 660–662, March 24, 1956. 7 refs.

In a study of the value of "nystatin" in preventing the growth of *Candida albicans* during antibiotic therapy, 50 male patients aged 12 to 81 years admitted to Ruchill Hospital, Glasgow, with pneumonia were allocated alternately to treatment with tetracycline alone and tetracycline plus nystatin. Tetracycline was given orally to both groups in a dosage of 0·25 g. 4-hourly for 48 hours and then 6-hourly for a further 3 days; nystatin was given as a sugar-coated tablet containing 500,000 units of nystatin once every 8 hours. Rectal and throat swabs and a specimen of sputum were taken on admission and again on the 3rd, 5th, 7th, and 9th days of treatment, these being inoculated directly on to plates of Sabouraud's medium, incubated at 37° C. for 48 hours, and then examined for growth of yeasts. If no growth had occurred, the plates were kept for a further 14 days at bench temperature before being classified as negative; growth was recorded as absent, scanty, or heavy. *C. albicans* was identified by the colonial and microscopical appearances and by fermentation reactions.

From one-quarter to one-third of the specimens taken on admission were found to contain *C. albicans*, the sputum yielding positive results more frequently (38%) than the rectal (26%) or throat swabs (24%). Treatment with tetracycline caused an increase in the number of specimens positive for *C. albicans*, the incidence gradually rising up to the 7th day of treatment. There was a definite trend towards the elimination of heavy growths from rectal swabs in the nystatin-treated group, but the effect on the throat was less obvious, while in regard to the sputum the two groups appeared to be similar. No patient developed side-effects in the group given the combined treatment.

The author concludes that these results are in keeping with the view that nystatin was not present in the blood in adequate concentration, and suggests that the antibiotic might be ineffective in the treatment of systemic infection. *Norval Taylor*

835. **Treatment of Cancer with Triethylene Thiophosphoramide and Oxapentamethylene**

J. C. BATEMAN and N. J. LARSEN. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] 4, 341–347, April, 1956. 5 refs.

In this paper from George Washington University, Washington, D.C., the authors summarize the results obtained in 195 patients with far-advanced cancer who were treated with two alkylating agents—N-N′-N″-triethylene thiophosphoramide and N-(3-oxapentamethylene)-N′-N″-diethylene phosphoramide. The former was given in a dosage of 5 to 40 mg. every one to 3 weeks and the latter in a dosage of 10 to 80 mg. at similar intervals for periods up to 485 days, the average duration of treatment with the two drugs being 89 and 36 days respectively. In addition to intramuscular, intravenous, and intra-arterial injection, the routes of administration included injection into the pleura, pericardium, peritoneum, and cranium, and direct injection into tumour masses. Of the 195 patients 122 received triethylene thiophosphoramide, 26 received the oxapentamethylene compound, and 47 were changed from one drug to the other.

Of the 65 patients with cancer of the breast, the commonest site, 57 were considered to show significant objective and/or subjective improvement. Of 19 with ovarian neoplasms 15 were improved, and of 16 with bronchial carcinoma, 10 were benefited; improvement was observed in all 5 patients with tumours of the central nervous system. Only in the three groups with tumours of the gastro-intestinal tract, melanomata, and miscellaneous lesions respectively did fewer than 50% of the patients improve.

Systemic toxicity included transient pyrexia, leucopenia, and thrombocytopenia; the oxapentamethylene compound occasionally caused bone-marrow depression, which might be sudden and severe. The clinical response to treatment was slow to manifest itself, continuous maintenance therapy, limited only by the possibility of haematopoietic depression, being necessary.

The authors consider that these cytotoxic phosphoramides are of value as palliatives in cases of advanced cancer, but that further study is necessary to define the limits within which they are of use therapeutically.

[The criteria of improvement are not described in detail and clinical summaries of only 2 cases are given. A more factual discussion of toxic reactions would have been helpful.] *Kenneth Gurling*

Infectious Diseases

836. **Treatment of Tetanus. Severe Bone-marrow Depression after Prolonged Nitrous-oxide Anaesthesia**
H. C. A. LASSEN, E. HENRIKSEN, F. NEUKIRCH, and H. S. KRISTENSEN. *Lancet* [*Lancet*] **1**, 527–530, April 28, 956. 4 figs., 8 refs.

Experience in the management of cases of poliomyelitis during the epidemic of the disease in Copenhagen in 1952 led the authors to try similar therapeutic measures—namely, sedation and curarization for prolonged periods with manually maintained artificial respiration—in cases of tetanus. To prevent the psychological strain of long periods of complete helplessness, narcosis was induced with a mixture of 50% nitrous oxide and 50% oxygen, nitrous oxide being considered harmless. In the present paper 7 cases of tetanus treated in this way are described. In the first 2 there was complete recovery, indicating that tetanus is a self-limiting disease if the exhausting spasms can be controlled. In the third case the tetanus subsided after 17 days' treatment and all sedatives except chloral were discontinued. Signs of aplastic anaemia then developed which, in spite of blood transfusions, proved fatal 2 weeks later. From a review of the clinical details of the first 2 cases it became clear that in these also there were signs of bone-marrow damage (haemorrhage and leucopenia).

In the subsequent cases in this series it was observed that the changes in the blood picture regularly appeared at an interval of 5 to 7 days after the introduction of nitrous oxide narcosis, there being signs of remission as soon as the administration of nitrous oxide was discontinued. The nitrous oxide available in Denmark is 99·7% pure, but the authors are convinced that there is a causal relationship and are now carrying out animal experiments to elucidate the problem.

During the period of the authors' observation of these cases Mollaret *et al.* published the report of a case similarly treated except that nitrous oxide was not used, in which agranulocytosis developed, though without aplastic anaemia.

Donald V. Bateman

837. **Ornithosis. An Analysis of 44 Human Cases with Positive Complement Fixation Tests**
M. B. JØRGENSEN and K. A. STEFFENSEN. *Danish Medical Bulletin* [*Dan. med. Bull.*] **3**, 20–24, Feb., 1956. 4 figs., 14 refs.

The authors analyse the features of 44 cases of ornithosis giving a positive response to the complement-fixation test which were seen at Blegdamshospitalet, Copenhagen, between 1952 and 1955. In 27 cases, Group A, the following criteria were satisfied: (1) the clinical features of an acute infectious disease; (2) a history of contact with birds within a reasonable time of the onset of the disease; and (3) a complement-fixation titre of 60 or more in at least one test. The remaining 17 cases in which these criteria were not satisfied constituted Group B. There were 14 males and 13 females in Group A and 10 males and 7 females in Group B, and the ages of the patients ranged from 20 to 80 years.

A distinct seasonal variation in the incidence of the disease was observed, the maximum incidence occurring in February, and over the period of the study there was a marked increase in the number of cases. The incubation period appeared to vary from about one week to 1½ months. The epidemiological and clinical features in the two groups revealed no significant differences. The clinical course was similar to that already described by other workers, but, the authors state, the classic, very severe picture seen in psittacosis was not encountered and there were no deaths. Radiological examination revealed signs of recent pulmonary involvement in 22 cases in Group A and 15 cases in Group B. In the former there were patchy infiltrations consistent with pneumonitis, but no pleural changes. In 2 cases in Group B pleural densities were noted; in the remaining 13 cases the radiological changes were interpreted as those of pneumonitis. Complications included thrombophlebitis, pyuria, microscopic haematuria, and transitory proteinuria. Pulmonary tuberculosis, hitherto undiagnosed, was found in 2 cases and cancer of the right lung in one.

The authors consider that a positive response to the complement-fixation test is practically always diagnostic of ornithosis or of some closely related disease which is indistinguishable from ornithosis in the absence of knowledge of the causative virus. *R. G. Meyer*

838. **Persistence of Abnormal Hepatic Tests in Carriers of Viral Hepatitis**
R. F. NORRIS, D. KASSOUNY, J. G. REINHOLD, and J. R. NEEFE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 1118–1121, March 31, 1956. 2 figs., 9 refs.

Since no laboratory method yet exists for the detection of the virus of infective hepatitis in the blood of carriers the effect of the carrier state on the results of liver function tests has been investigated by the authors at the University of Pennsylvania, Philadelphia, in the hope of finding an alternative means of eliminating potentially infective blood donors. In a previous paper (Neefe *et al.*, *J. Amer. med. Ass.*, 1954, **154**, 1066; *Abstracts of World Medicine*, 1954, **16**, 190) they described the occurrence of hepatitis in 14 cases after blood transfusion and their investigation of the 22 donors concerned, resulting in the detection of the carrier state in 5 of them by transmission of the infection to human volunteers. They now report the results of repeated liver function tests carried out over a period of 4 years on these 5 and on 15 of the remaining 17 donors. These tests included estimation of the serum bilirubin level, the thymol

turbidity, thymol flocculation, cephalin–cholesterol flocculation, and zinc turbidity tests, and estimation of the urinary urobilinogen content and of " bromsulphalein " retention.

The results observed for each donor, whether normal or abnormal, were consistent throughout the period. All the proved carriers gave an abnormal result in at least one of the tests, and in no case where the recipient had received blood from only one donor were the results of all tests on that donor normal. But of 4 additional cases of hepatitis following a single transfusion, in 3 the results of tests on the donor were normal at the time of the transfusion. Taking the thymol turbidity and thymol flocculation tests alone, 4 donors out of 15 whose blood was undoubtedly responsible for hepatitis in the recipient gave normal results. It would therefore appear that any screening procedure based on these tests cannot be wholly effective.

It has been suggested that sufferers from clinically apparent viral hepatitis may be carriers during their convalescence, but should be acceptable for transfusion after their complete recovery because of the presence of antibodies in their blood. However, serum from one of the original donors who subsequently himself developed hepatitis was still infectious to volunteers 6 months after his clinical recovery. *E. Forrai*

839. **Serum Glutamic Oxalacetic Aminopherase (Transaminase) in Hepatitis**

F. Wróblewski and J. S. LaDue. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 1130–1134, March 31, 1956. 18 figs., 7 refs.

It has been demonstrated that acute myocardial infarction and hepatitis due to toxic or infective agents cause a rise in the serum glutamic oxalacetic aminopherase (transaminase) activity to 2 to 20 and 20 to 100 times the normal level respectively. In patients with infectious, neoplastic, degenerative, reactive, allergic, or congenital disease states on the other hand there is no rise in serum transaminase level unless there is acute damage to the liver, heart, or skeletal muscle. In this paper from the Memorial Center for Cancer and Allied Diseases, New York, the authors describe observations on serum transaminase activity made during the course of an epidemic of infective hepatitis which occurred in an institution for the mentally defective, and compare them with similar observations made in cases of liver disease of other types.

It was shown that the serum transaminase activity rises one to 4 weeks before other clinical or laboratory signs of liver injury become manifest. This allows the diagnosis of hepatitis to be made in the pre-icteric stage and gives an opportunity for the early isolation of contacts. Measurements of serum transaminase activity also enables jaundice due to hepatitis to be differentiated from that due to cirrhosis, extrahepatic obstruction of the biliary ducts, liver metastases, or haemolysis. An increase in the serum transaminase level also precedes the development of jaundice in patients undergoing treatment with potentially hepatotoxic drugs. In hepatitis the transaminase activity in the serum seems to correspond more closely to the clinical picture than the serum bilirubin level, which may remain elevated for a long time after clinical improvement has begun and the transaminase level has fallen. *E. Forrai*

840. **World-wide Geographic Distribution of Histoplasmosis and Histoplasmin Sensitivity**

P. Q. Edwards and J. H. Klær. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **5**, 235–257, March, 1956. 1 fig., bibliography.

Histoplasmosis is no longer the rare and fatal disease it was once thought to be. Infection due to *Histoplasma capsulatum* is now known to be widespread in some parts of the world, but clinical symptoms develop in only a few infected subjects. Histoplasmosis in its pulmonary forms closely resembles tuberculosis of the lungs, the calcification and fibrotic scars seen in the chest radiograph being indistinguishable from those observed in tuberculosis. Skin tests have shown that a large proportion of subjects living in certain areas react strongly to histoplasmin, an antigen prepared from broth cultures of *H. capsulatum*.

The authors of this paper from the U.S. Public Health Service, Washington, D.C., and the W.H.O. Tuberculosis Research Office, Copenhagen, have attempted to bring together information collected from a number of sources on the prevalence of histoplasmosis and of histoplasmin sensitivity in various parts of the world. A map shows wide areas in the United States in which the incidence of positive reactors to histoplasmin sensitivity tests is 20% or higher, a figure which is equalled in a few selected areas in South America and Asia. In certain areas of Africa and in other areas of Asia and the American continent the incidence is 10% or more, but for many parts of the world there is no information to indicate whether or not histoplasmosis is a significant health problem.

Factors which suggest the existence of an endemic focus of infection are: (1) the occurrence of cases in which the diagnosis is confirmed by culture of the organisms, especially if the patients are life-time residents of the locality; (2) cutaneous sensitivity to histoplasmin in the population; and (3) correlation between histoplasmin sensitivity and *x*-ray evidence of pulmonary infiltration or of calcified residual lesions. Airborne spread of contaminated soil appears at present to be the method of transmission of the disease.

From the findings it is concluded that histoplasmosis is primarily a disease of the American Continent; that it may also exist in an endemic form, but " presumably at a much lower prevalence ", in some parts of Africa and south-eastern Asia; and that " there is little indication of the existence of infection with *Histoplasma* in Europe, the Eastern Mediterranean, and those parts of Asia from which information is accessible ".

R. R. Willcox

841. **A Roentgenographic Study of Skeletal Lesions in Sarcoidosis**

G. N. Stein, H. L. Israel, and M. Sones. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **97**, 532–536, May, 1956. 5 figs., 7 refs.

Tuberculosis

842. **A Comparative Study of the Treatment of Tuberculosis of the Kidney.** (Vergleichende Behandlungsergebnisse der Nierentuberkulose)
R. HOHENFELLNER and W. LORBEK. *Tuberkulosearzt* [*Tuberkulosearzt*] **10**, 211–216, April, 1956. 11 refs.

Of 66 cases of renal tuberculosis seen at the 2nd Surgical Clinic, University of Vienna, during the last 17 years, 45 were treated in the pre-chemotherapeutic era (1938–48) and 21 in the period 1949–54. In the earlier period 37 patients underwent unilateral nephrectomy and 8 were treated medically; of the former, 17 were cured, 5 were not cured, 9 died, and 6 were lost to follow-up, while of the latter, 2 were cured, 4 died, and 2 could not be traced. In the more recent period, of 15 patients subjected to nephrectomy and chemotherapy, 13 were cured, one was not benefited, and one died, while of 6 treated by chemotherapy alone, 5 were cured and one not. Thus the over-all probable cure rates in the two periods for treatment with and without nephrectomy were 42 and 86% respectively.

Partial nephrectomy was not employed, the authors' reasons against it being that with good drainage of the upper pole it is unnecessary, that when radiological evidence is negative the presence of foci may be demonstrated histologically, and thirdly that no long-term results of the operation are as yet available. Reserving streptomycin for preoperative treatment, the authors gave a 4-week course of 10 to 15 mg. of isoniazid per kg. body weight daily (divided in 4 doses), alternating with a 4-week course of 8 to 12 g. of PAS combined with 1 to 1·5 mg. of " conteben " (thiacetazone) per kg. body weight daily. *R. Crawford*

843. **Tuberculin in Aqueous and Oily Solutions. Skin-test Reactions in Normal Subjects and in Patients with Sarcoidosis**
D. G. JAMES and J. PEPYS. *Lancet* [*Lancet*] **1**, 602–604, May 5, 1956. 15 refs.

At the Middlesex Hospital Medical School, London, the authors have investigated and compared the skin-test reactions to aqueous tuberculin and tuberculin in oily emulsion in a number of Mantoux-positive, Mantoux-negative, and B.C.G.-vaccinated normal subjects, and in patients suffering from sarcoidosis. The injections were made into the skin of the upper arm and control tests showed that reactions caused by the oily vehicle alone were negligible.

In 5 Mantoux-positive normal subjects the reaction obtained with 10 units of aqueous tuberculin was similar to that with 5 T.U. of oily suspension, while 18 normal persons who were Mantoux-negative to 100 T.U. of aqueous tuberculin were also negative to 5 T.U. of the oily preparation. The 9 subjects given B.C.G. vaccination had been repeatedly negative to tests with 100 T.U. of aqueous tuberculin. They were given an injection of oily tuberculin 4 weeks before vaccination and a Mantoux test with 100 T.U. of aqueous tuberculin 6 weeks afterwards; 4 gave positive reactions to both types of tuberculin, 2 to the oily tuberculin only, none to the aqueous tuberculin only, and 3 gave negative reactions to both types. In 6 of the 9 subjects a reaction appeared at the site of the previously negative test with oily tuberculin some 10 days after the B.C.G. vaccination and remained unchanged for about 2 months. Of 23 patients with sarcoidosis of varying degrees of activity, 4 reacted positively to both preparations and 13 to the oily tuberculin only.

The authors suggest that the long local persistence of the antigen in the oily " depot tuberculin " enables a lower degree of sensitivity to tuberculin to be detected than is possible with aqueous tuberculin.

John M. Talbot

844. **Experience with the Tuberculostatic Drug " Vionactan " [Viomycin] Pantothenate.** (Erfahrungen mit dem Tuberculostaticum Vionactanpantothenat)
J. KOCH. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **86**, 413–415, April 21, 1956. 25 refs.

The author has found that the administration of viomycin in the treatment of tuberculosis, even in a reduced dosage of 2 g. twice weekly, is still apt to cause minor reactions, such as pain at the injection site, nausea, eosinophilia, skin rashes, occasional albuminuria with the appearance of blood cells and casts in the urine, and febrile reactions. In the present paper from the Midi Sanatorium, Davos, Switzerland, he compares the results in 6 patients who were given 1 g. of viomycin every other day in two injections of 0·5 g. with those obtained in 37 patients who received a similar dose of viomycin in the form of its pantothenate, " vionactan P ". All patients were concurrently treated with streptomycin, PAS, or isoniazid, or a combination of two of these drugs. In 6 cases viomycin was also injected intrapleurally in a dose of 0·5 g. daily or every other day, and in one case of tuberculous osteitis a solution of the drug was applied to the sinuses. The total dose of viomycin ranged from 7 to 48 g. The 43 cases included 14 cases of chronic pulmonary tuberculosis, mostly progressive, 7 recent cases of pulmonary disease, 2 cases of bone and joint tuberculosis, one each of tuberculous meningitis, miliary tuberculosis, and urogenital tuberculosis, and 17 postoperative cases subjected to various surgical procedures under antibiotic cover.

Of the chronic cases, in only 2 did the sputum become negative, although general improvement was noted in 8 cases and radiological improvement in 6. As might have been expected, the results in the more recent cases were more favourable, nearly all of them improving under the treatment, some markedly so. [The follow-up

period is, however, not stated, and in 7 cases the course of viomycin had not been completed at the time of the report.] Of the 17 postoperative patients, 12 made good progress, but 2 developed a broncho-pleural fistula and one contralateral spread of the disease. No severe side-reactions were noted, although in 2 cases in each group the drug had to be discontinued, in 3 because of an intractable urticaria and in one on account of a supervening infection with *Escherichia coli*. Milder reactions were noted in 12 of the 37 patients given vionactan P and in 5 of the 6 patients receiving viomycin; these included mild pyrexia, nausea, skin rashes, and transient albuminuria. Eosinophilia was noted in 18 cases in all.

The author considers that viomycin pantothenate is a useful addition to the range of antituberculous drugs, that it is comparable in efficacy to PAS and isoniazid, and that it is particularly suitable for local therapy in cases of tuberculous empyema. *H. F. Reichenfeld*

845. **The Treatment of Forty Cases of Tuberculosis of the Pleura, Lung, or Lymph Nodes with Adrenocortical Hormones in Association with Antituberculous Drugs.** (A propos de 40 cas de tuberculoses pleurales, pulmonaires ou ganglionnaires traités par corticothérapie surrénalienne, associée aux antibiotiques antibacillaires)
Y. Rose and Y. Jauffret. *Poumon et le Cœur* [*Poumon et Cœur*] **12**, 223–234, March, 1956.

During the last 2 years at the Hôpital de Lagny, Seine-et-Marne, the authors have treated 40 cases of tuberculosis of the pleura, lungs, and lymph nodes with PAS, streptomycin, and isoniazid in combination with either corticotrophin (ACTH) or cortisone (or both in alternate courses) and are of the opinion that these hormones are of value in tuberculosis and not dangerous to tuberculous patients as has been thought. The patients were of both sexes and ranged in age from 9 to 63 years. The routine daily dosage of antituberculous drugs given over the customary period was 15 g. of PAS with 1 g. of streptomycin and 5 mg. of isoniazid per kg. body weight. Either ACTH, 5 to 12 mg. daily by infusion with the PAS solution for 10, 15, or 30 days according to effect, was given or else 50 to 100 mg. daily of cortisone by mouth (or hydrocortisone, 40 to 60 mg. daily) together with a weekly intramuscular injection of 50 mg. of testosterone acetate. Intolerance to one or other of the antituberculous agents occurred in 7 patients and was overcome in every case by the addition of ACTH or hydrocortisone in minimum doses of 5 mg. daily. No case of salt retention or any untoward incident occurred.

In 26 cases good results were obtained (in at least 12 of which antituberculous drugs alone had previously proved unsatisfactory); these included 4 cases of serofibrinous pleurisy (2 acute, one subacute, and one chronic), 6 cases of pleural effusion following intrapleural pneumothorax, 5 cases of pleurisy associated with a lung lesion, one of acute miliary disease, 2 of caseating pneumonia, 5 of chronic ulcero-nodular lesions and one each of discrete rounded foci, diseased mediastinal nodes, and diseased cervical nodes. Of the remaining 14 cases, there was no improvement in 9; in 3 cases the result might have been equally good without adrenocorticotherapy, while in the remaining 2 improvement was only transitory. These 14 cases included 7 of chronic pleural effusion, 6 of chronic ulcero-nodular lesions, and one of a discrete rounded lesion. The authors suggest that by reducing acute inflammatory reactions the hormonal adjuvant facilitates the action of antituberculous drugs upon the tuberculous lesions and further often allows the intensive use of these agents when they might not otherwise be tolerated.
V. Reade

RESPIRATORY TUBERCULOSIS

846. **Air Embolism during Pneumoperitoneum Treatment**
D. Burman. *Thorax* [*Thorax*] **11**, 49–56, March, 1956. 3 figs., bibliography.

In this paper from the Tan Tock Seng Hospital, Singapore, the literature concerning air embolism during induction of pneumoperitoneum is reviewed and 6 new cases are reported, one occurring in the course of 926 inductions and 5 during 53,534 refills. From an analysis of all published cases, including the present series, the incidence of air embolism during induction is estimated as 1 in 437 and during refills as 1 in 9,000, while the over-all mortality appears to be 41·5%. The author suggests that these figures probably overestimate the true frequency of this complication and the case fatality.

The commonest causes of air embolism are inexperience on the part of the operator and insertion of the needle too high in the abdomen. Air was introduced into the liver or spleen in 10 of the 53 published cases. In the treatment of air embolism the patient must be immediately placed in a steep head-down position, turned on the left side, and given 100% oxygen from a closely fitting mask, this position being maintained for 2 to 3 hours. *E. Keith Westlake*

847. **Bed Rest in the Treatment of Pulmonary Tuberculosis**
W. F. Tyrrell. *Lancet* [*Lancet*] **1**, 821–823, June 2, 1956. 2 refs.

An attempt was made at Ruchill Hospital, Glasgow, to determine whether rest in bed is essential in the treatment of patients suffering from pulmonary tuberculosis. Of 141 patients in whom the disease was newly diagnosed, 71 were admitted to hospital, where treatment included strict rest in bed, while 70 were allowed to follow their normal routine at home; all the patients received chemotherapy with streptomycin and isoniazid. Of the in-patients, 34 were males, average age 29·5 years, and 37 were females, average age 24·6 years; of the out-patients, 33 were males, average age 30 years, and 37 were females, average age 27·5 years.

After 3 months' treatment there was no significant difference between the two groups in such factors as reduction in the erythrocyte sedimentation rate (E.S.R.), sputum conversion, cavity closure, and over-all radiological improvement. At the end of 6 months, progress was assessed in 45 of the in-patients and 46 of the out-

patients; again no difference was observed between the two groups as regards reduction in E.S.R., sputum conversion, and over-all radiological improvement, but cavity closure was a more frequent finding in the former group than in the latter. At the start of treatment cavitation was present in 36 in-patients and 44 out-patients; at the end of the 6 months cavities were present in 26 patients in each group.

Kenneth M. A. Perry

848. **Clinical Observations on the Effect of Aerosols of Isoniazid and Streptomycin in the Treatment of Pulmonary Tuberculosis.** (Klinische Beobachtungen über die Wirkung von INH- und Streptomycin-Aerosolen in der Behandlung der Lungentuberkulose)
G. PICKROTH. *Zeitschrift für Tuberkulose* [*Z. Tuberk.*] 108, 9–14, 1956. 42 refs.

At the University Chest Clinic, Jena, East Germany, 67 patients, all with extensive pulmonary tuberculosis which had failed to respond satisfactorily to prolonged chemotherapy with systemic PAS and isoniazid and all but 5 of whom had a persistently positive sputum, were treated with inhalations of isoniazid or streptomycin for periods of 30 days at a time, the systemic administration of drugs being continued during this time. Isoniazid was used in a 4% solution, aerosol containing 40 mg. being inhaled 3 times a day, while another containing 0·5 g. of streptomycin in water was inhaled twice a day.

Of 57 patients with positive sputum who completed at least one course, 11 derived great benefit and 12 significant benefit, in the sense that their sputum became negative for varying periods of time.

[However, no case appears to have been followed for more than 6 months from the date of the last course of inhalations, and no mention is made of any effects of the treatment on other aspects of the disease, in particular on the radiological appearances. In a very few of the cases there was evidence that the reappearance of viable tubercle bacilli in the sputum after an initially successful course of inhalations was not associated with resistance to the drug inhaled.] *P. Mestitz*

849. **Preliminary Clinical Trials of Dihydrostreptomycin Pantothenate.** (Premiers essais cliniques du pantothénate de di-hydrostreptomycine)
R. LESOBRE and H. VERNEY. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] 72, 227–237, March 2, 1956. 6 refs.

In order to avoid the toxic effects of dihydrostreptomycin the authors have tried "6724 R.P.", one gramme of which contains 800 mg. of dihydrostreptomycin sulphate and 200 mg. of dihydrostreptomycin pantothenate, in the treatment at the Hôpital Broussais, Paris, of 8 patients seriously ill with pulmonary tuberculosis, some of whom had already become resistant to chemotherapy; the drug was given in doses of 1 to 3 g. daily to totals ranging from 46 to 340 g. All patients except one benefited appreciably from the treatment, 2 (a man aged 26 and a girl aged 16) being able to undergo Blalock's operation for coincident Fallot's tetralogy. However, 3 patients developed auditory nerve impairment after doses of 46, 150, and 180 g. respectively of 6724 R.P., but the first of these patients had already received 115 g. of dihydrostreptomycin. In contrast, one patient who had previously received 92 g. of dihydrostreptomycin was able to tolerate a further 340 g. of 6724 R.P. in a dosage of 2 g. daily without any toxic manifestations. Brief histories of the 8 cases are given. *I. Ansell*

850. **The Value of Dihydrostreptomycin Pantothenate in the Prevention of Complications in the Intensive Treatment of Tuberculosis.** (Intérêt du pantothénate de dihydrostreptomycine dans la prévention des accidents au cours des traitements intensifs de la tuberculose)
J. CÉLICE, M. AUBRY, F. PLAS, and G. DUCHESNAY. *Bulletins et mémoires de la société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] 72, 237–246, March 2, 1956. 13 refs.

After a preliminary review of the literature on the toxic effects of intensive streptomycin therapy and the various methods adopted to counteract these effects, the authors record the results achieved in the treatment of 4 female tuberculous patients with "6724 R.P." (dihydrostreptomycin pentothenate) at the Hôpital Saint-Antoine, Paris. One patient aged 70 years with a tuberculous pleural effusion had begun to experience vertigo after receiving a total of 15 g. of dihydrostreptomycin; this became more marked after 36 g. but began to improve on cessation of therapy; a further 31 g. of 6724 R.P. produced no recurrence of the vertigo. Another patient aged 65 years with bilateral fibro-caseous pulmonary tuberculosis who developed vertigo after 55 g. of dihydrostreptomycin received 30 g. of 6724 R.P. without any aggravation of the vertigo—which indeed began to diminish. A third patient aged 53 years with extensive bilateral cavitating disease received 210 g. of 6724 R.P. in 82 days without toxic effects. The last patient, a young woman of 21 with tuberculous bronchopneumonia complicating a primary infection, received 120 g. of 6724 R.P. in 60 days without any evidence of damage to the auditory nerve. All the patients benefited from the treatment, especially those receiving 2 to 3 g. daily a dosage not possible with dihydrostreptomycin alone.

I. Ansell

851. **"Gatalone" in the Treatment of Pulmonary Tuberculosis**
E. J. DES AUTELS, K. H. PFUETZE, J. R. ZVETINA, C. A. COLWELL, A. R. HESS, and C. J. WOODS. *Diseases of the Chest* [*Dis. Chest*] 29, 357–365, April, 1956. 3 figs., 16 refs.

The therapeutic effects of "gatalone" (D-glucuronolactone *iso*nicotinyl hydrazone; INH-G) in 11 cases of pulmonary tuberculosis were evaluated at the Veterans Administration Hospital, Hines, Illinois. None of the patients had had chemotherapy previously and all had exudative disease with cavitation. The drug was given in a dosage of 1,600 mg. daily (an isoniazid content of 732 mg.) for at least 6 months. In 2 patients, however, the dosage was reduced because of neuropathy.

A good clinical response was obtained in all the cases although there was a relapse in 2. Considerable radio-

logical improvement was noted in 6, with cavity closure in 2; sputum conversion occurred in 3 cases. However, symptoms and signs of peripheral neuropathy developed in 7, these being moderately severe in 2. In 4 patients there was a slight rash.

The authors do not consider that gatalone in the dosage employed in this series is superior therapeutically to 300 mg. of isoniazid daily; the incidence of neuropathy, however, is much higher. It is suggested that since the drug is excreted as active INH-G and free isoniazid it may have a beneficial effect in renal tuberculosis. A trial of this drug in a lower dosage is recommended. *Paul B. Woolley*

852. **The Treatment of Exudative Pleurisy with Topical Hydrocortisone Combined with Antimycobacterial Therapy.** (Trattamento delle pleuriti essudative con idrocortisone per via topica in associazione con terapia antimicobatterica)

M. Reale, A. Garaventa, and G. Paoli. *Minerva medica* [*Minerva med. (Torino)*] **1**, 798–804, March 21, 1956. 18 refs.

The authors recommend the treatment of exudative pleurisy in the acute stage by the injection into the pleura of a single dose of 50 to 75 mg. of hydrocortisone after aspiration of the fluid, which is usually immediately effective. In subacute cases they give daily intravenous infusions of ACTH (corticotrophin), an initial dose of 5 mg. being followed by doses decreasing to 1 or 0·5 mg. The duration of the treatment depends upon the rate of disappearance of the exudate and the fall of temperature and erythrocyte sedimentation rate. In both cases the hormone treatment is associated with treatment with streptomycin or isoniazid. *Franz Heimann*

853. **A Review of 138 Cases of Closure of Tuberculous Lung Cavities under Chemotherapy**

J. D. Ross and D. T. Kay. *Thorax* [*Thorax*] **11**, 1–9, March, 1956. 4 figs., 31 refs.

The authors at the University of Edinburgh examined the records of all adult patients discharged from three tuberculosis units between January, 1952, and December, 1954, with the object of determining the frequency with which cavity closure was achieved with chemotherapy (usually a combination of streptomycin with PAS or isoniazid) and a sanatorium regimen. All lung cavities were closed with chemotherapy in 138 out of a total of 745 cases. In 97 of these 138 chemotherapy had been discontinued, and these cases are analysed in detail in this paper.

Among 55 patients who received no further treatment the annual relapse rate was 5·9%. Among the remaining 42 patients, who underwent various operations (lung resection in 18, thoracoplasty in 6, pneumoperitoneum in 17, and artificial pneumothorax in 1), the annual relapse rate was 3·3%. The relapse rate in the two groups was small and the difference between them was not significant. No definite correlation was found between the size of residual lumps and the incidence of relapse. The duration of chemotherapy appeared to be the most important factor; no relapses occurred in patients who received chemotherapy for more than 8 months after cavity closure.

Of one group from one unit of 115 patients with lung cavitation initially complete closure was obtained with chemotherapy in 58, an observed closure rate of 50%. A progressive increase in this rate was noted when chemotherapy was continued for 8 months. The authors estimate that closure of tuberculous cavities may be expected in 50 to 79% of cases treated with chemotherapy alone.

[This is an important paper. The value of surgery in the management of patients who have received a prolonged course of chemotherapy needs evaluation in a controlled clinical trial.] *E. Keith Westlake*

854. **The Post-mortem Bacteriology of Pulmonary Tuberculosis after Treatment with Specific Antibacterial Agents.** (Ulteriore contributo allo studio batteriologico dei pazienti deceduti per tubercolosi polmonare e trattati con chemio-antibiotici specifici)

M. Lucchesi, M. Zubiani, and G. Storniello. *Rivista della tubercolosi e delle malattie dell'apparato respiratorio* [*Riv. Tuberc.*] **3**, 577–593, Nov.–Dec., 1955 [received April, 1956]. 2 figs., 16 refs.

The authors have performed bacteriological studies post mortem on the pulmonary lesions of 100 patients dying from pulmonary tuberculosis who had received antibiotic treatment at the Forlanini Institute, Rome. Positive cultures of tubercle bacilli were obtained by Petragnani's method or in guinea-pigs in 81 cases altogether. Of 58 solid lesions examined, 42 (72%) yielded positive cultures, one-quarter of the organisms being avirulent, two-thirds resistant to streptomycin, and one-third resistant to isoniazid in various concentrations. Of 29 cavities examined, 25 (86%) yielded positive cultures, in only 2 of which were the organisms avirulent, while three-quarters were resistant to streptomycin and nearly one-half to isoniazid. Of 80 specimens of " para-hilar " lymph nodes examined, 51 (64%) gave positive cultures, four-fifths of the strains isolated being virulent, while resistance to streptomycin was present in two-thirds and to isoniazid in only one-fifth.

Among the conclusions which they draw, the authors deduce the superiority of isoniazid over streptomycin in the treatment of solid lesions and particularly in cases of lymph-node involvement which, they claim, is very frequent in post-primary tuberculosis. They state [without giving details] that there was little evidence of correlation between the type of chemotherapy given and the degree of resistance found post mortem. *Arnold Pines*

855. **Studies on the Constituents of *M. tuberculosis* Responsible for the Establishment of Resistance against Infection. 3. On the Inhibitory Effects of Bacterial Substance Isolated from Tubercle Bacilli on the Development of Experimental Tuberculosis**

Y. Takeda and K. Kiuchi. *Japanese Journal of Tuberculosis* [*Jap. J. Tuberc.*] 3, 87–100, Dec., 1955 [received Aug., 1956]. 8 figs., 18 refs.

Venereal Diseases

856. **Serological, Nephelometrical, and Statistical Studies on the Employment of Synthetic Lecithin in Cardiolipin Antigens**

A. REYN, M. W. BENTZON, and J. HARTMANN. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **32**, 40–46, March, 1956. 5 figs., 30 refs.

The effect of varying the cardiolipin:lecithin ratio while maintaining constant the cardiolipin and cholesterol concentration (thus involving also a variation in the absolute lecithin concentration) was investigated at the State Serum Institute, Copenhagen, in quantitative complement-fixation experiments on samples of syphilitic and non-syphilitic serum. In addition, nephelometric measurements were made of the light-scattering effects of the various antigen suspensions used, including registration of maturation curves. Furthermore, the keeping qualities of the antigens containing various concentrations of synthetic lecithin were compared in complement-fixation and V.D.R.L. slide flocculation tests with those of antigens containing natural egg lecithin. The effects of storage at room temperature for about 6 months, and at 56° C. for about 4 months, were also investigated. The serological and nephelometric results were subjected to statistical analysis.

The authors conclude that when synthetic lecithin is substituted for natural egg lecithin it is impossible to obtain a complement-fixation antigen of exactly the same sensitivity for all sera; that is, the same average sensitivity can be obtained, but the ratio between titres of individual sera are changed. However, they feel that the present results encourage further investigations with other batches of synthetic lecithin. *R. R. Willcox*

857. **The Clinical Value of the Quantitative Cardiolipin Microflocculation (V.D.R.L.) Test in the Serodiagnosis of Syphilis.** (Il valore clinico dell'analisi quantitativa con la microflocculazione cardiolipinica (V.D.R.L.) nella sierodiagnosi della lue)

G. GIOVANNELLI. *Igiene moderna* [*Igiene mod.*] **41**, 69–130, Jan.–Feb., 1956. 62 figs., 24 refs.

The author comments favourably on the recommendation of the Expert Committee of the World Health Organization that the results of serological tests for syphilis should be recorded simply as positive, negative, or doubtful, but points out that the clinician still needs a quantitative test in order to assess progress and the efficacy of treatment. At the Ospedale S. Niccolò, Siena, he carried out the quantitative V.D.R.L. microflocculation slide test with the cardiolipin antigen on sera from 32 patients with neurosyphilis before and after treatment, the results, where positive, being presented in the form of a graph, the dilution of serum being plotted as the abscissa and the degree of positivity (ranging from 1 to 5) as the ordinate. The other tests which were carried out on each serum included the Wassermann, M.K.R.II., and citochol reactions, but the results of these tests did not show the effect of treatment so clearly as did those of the V.D.R.L. test.

The simple graphic method of presentation of the results of the V.D.R.L. test in various dilutions shows clearly that sera giving the same result undiluted may give quite different titres of positivity when diluted. It also shows the occasional zone phenomenon, when serum at one dilution gives a higher degree of positivity than the undiluted serum, this peak disappearing under treatment. The test is technically easy, can be applied to cerebrospinal fluid, and uses a chemically well-defined antigen. The sera are diluted in tubes, and a drop from each dilution is mixed on a slide with a drop of antigen, agglutination being read both macro- and microscopically. *F. Hillman*

858. **Complement-fixation Titres in Tertiary Lymphogranuloma Venereum. A Study of Results after Treatment with Broad-spectrum Antibiotics**

J. GOLDBERG and L. BANOV. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **32**, 37–39, March, 1956. 4 refs.

In the study here reported from the Medical College of South Carolina, 14 negro patients (13 women and one boy) who were suffering from rectal involvement and stricture due to tertiary lymphogranuloma venereum were treated with one of the following antibiotics: oxytetracycline, chlortetracycline (aureomycin) chloramphenicol, or erythromycin. Complement-fixation tests were carried out before therapy and again between 12 and 27 months after treatment. In 7 cases there was no significant change in titre, while in the other 7 there was a 4-fold decrease in titre, although in 4 of the latter the residual titre was 1 in 40 or higher in spite of clinically satisfactory results.

It is concluded that positive reactions to a titre as high as 1 in 640 do not necessarily indicate an active infection with the virus—in so far as activity of the virus may be judged by the clinical symptoms. Nor can diminishing complement-fixation titres be used to establish a retrospective diagnosis of the disease even after clinically successful treatment with the broad-spectrum antibiotics. Some of the problems in the diagnosis of lymphogranuloma venereum are discussed.

R. R. Willcox

859. **Value of Treatment in Reiter's Disease**

W. FOWLER and G. H. KNIGHT. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **32**, 2–6, March, 1956. 21 refs.

The effect of various types of treatment has been assessed in 70 cases of Reiter's disease. The duration of the illness was no shorter than in 5 untreated cases, and we have found no evidence that any form of therapy at present in use has any influence upon the course of the illness.—[Authors' summary.]

Tropical Medicine

860. **Megaloblastic Anaemia of Infancy in Kwashiorkor and Other Diseases**
F. WALT, S. HOLMAN, and R. G. HENDRICKSE. *British Medical Journal* [*Brit. med. J.*] **1**, 1199–1203, May 26, 1956. 13 refs.

Between February, 1954, and February, 1955, the 776 children, mostly Bantu and the majority under 3 years of age, admitted to the McCord Zulu Hospital, Durban, were examined with the possibility of megaloblastic anaemia in mind. Nearly all the patients came from homes where nutrition was poor and infections frequent. All cases showing a "suggestive clinical picture" or with a haemoglobin level below 6·7 g. per 100 ml. were investigated by repeated bone-marrow and blood-film examinations and haemoglobin and reticulocyte estimations. Megaloblastic anaemia was found in 42 cases (5·4%), in 22 of which there was typical kwashiorkor. The diagnosis was made solely on marrow examination, megaloblasts being diagnosed only if the nuclear chromatin showed a "lacy" pattern, "scroll-work", or "woven-skein" appearance. Supporting subsidiary evidence was enlargement of nucleated erythrocytes, marked disproportion in size between nucleus and cytoplasm, the finding of Howell–Jolly bodies, and trefoil and clover-leaf nuclei in the nucleated erythrocytes. Nearly all the megaloblastic marrow smears also showed altered granulocytes in the form of bizarre myelocytes, metamyelocytes, and bizarre giant "stab" cells. The peripheral blood often contained megaloblasts and large, multilobed, polymorphonuclear leucocytes (though prolonged search might be needed), while macrocytosis and ovalocytosis was common; the most valuable single diagnostic factor was the haemoglobin value, which in almost every case was below 7·4 g. per 100 ml.

Clinically, the patients could be divided into three types. (1) Those severely anaemic on admission (haemoglobin level less than 5 g. per 100 ml.); these were usually suffering from infection or kwashiorkor, or both, and were extremely ill. (2) Those who developed their anaemia insidiously while the primary disease was being treated; in this group the haemoglobin value averaged 6 to 7 g. per 100 ml. (3) Those developing an acute severe anaemia (haemoglobin level 3 to 4 g. per 100 ml.) with a palpable spleen. In none of the patients were malaria or worm infestation present to any significant extent. Treatment consisted in the oral administration of folic acid, 5 mg. three times a day followed by 5 mg. daily for one month after discharge from hospital; in 8 cases one injection of 7·5 mg. of folic acid was also given intramuscularly, and 2 cases were treated with cyanocobalamin (vitamin B_{12}). Blood transfusion was given in 22 cases, and other treatment included antibiotics, intravenous therapy, and administration of skimmed milk, streptomycin, isoniazid, and corticotrophin (ACTH).

Of the 42 patients, 10 died, 8 of these having a haemoglobin level on admission of under 6·7 g. per 100 ml. Only one death, from an acute anaemic crisis, was attributed to the anaemia itself, the rest being from the primary illness. Of the 15 patients who developed an acute anaemic crisis, 13 survived, probably mainly owing to prompt blood transfusion. Improvement was assessed by noting improved appetite, weight gain, and general appearance and behaviour. Although a reticulocyte response of over 8% ultimately occurred in 30 of the 34 patients in which this was measured, the response was not uniform, and the haemoglobin level usually rose only slowly, many children leaving hospital with a lower haemoglobin value than on admission. Discussing the relatively high incidence (5·4%) of megaloblastic anaemia in this series, the authors contrast it with the low incidence reported elsewhere; they suggest that an increased awareness of the condition may possibly be one factor. They consider the anaemia to be secondary to malnutrition and/or infection (especially gastro-enteritis, pneumonia, or otitis media). It responds well to folic acid, which is thought to be specific mainly because there is rapid disappearance of megaloblasts from the marrow following its administration. Ascorbic acid is not thought to be a significant therapeutic factor, but the exact roles played by intramuscular folic acid (where absorption of oral folic acid is impaired) and by cyanocobalamin have yet to be determined.

[The original article should be referred to for details of the individual cases.] *M. Kendal*

861. **Observations on the Cytology of Gastric Epithelium in Tropical Sprue**
F. H. GARDNER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **47**, 529–539, April, 1956. 4 figs., 11 refs.

862. **Eradication of Tick-borne Relapsing Fever in the Somaliland Protectorate by a Tick Destruction Programme**
W. C. D. LOVETT. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **50**, 157–165, March, 1956. 1 fig., 13 refs.

Relapsing fever has been indigenous to the Somaliland Protectorate, a semi-desert country, for as long as is known, the common if not the sole vector being *Ornithodorus moubata*, an infestant of the coffee shops and mat huts used by nomadic Somali in the towns, where the incidence of the disease is high. Before 1949 the cost of solvents for insecticides, not the insecticides themselves, precluded any large-scale prophylaxis, but in that year a water-dispersable product, "gammexane P.520", was introduced and found to be both effective and economical to apply. At Burao, a township of some 2,000 native "buildings" which was known to be

one of the chief centres of infection, the insecticide, in dilutions of 12 oz. to the gallon (75 g. per litre), was sprayed by stirrup pumps fitted with special lime-washing nozzles over floors and the lower 18 inches (45 cm.) of walls, one gallon (4·5 litres) being used for roughly 1,200 to 1,500 square feet (112 to 140 sq. metres). The spraying was repeated after an interval of 4 to 6 weeks, and later carried out in other parts of the country. The total cost of the campaign was less than £400.

In 1946 there were 488 known cases of relapsing fever in Burao and 625 in the whole country; by 1953 there were no known cases in any part of the Protectorate. (There had been a considerable fall in incidence before the intensive spraying was started, but this is not considered to lessen the value of the campaign.) The author states that this form of control prevents reintroduction of the disease on any scale; the vector tends to live in or near its hatching place, so that its re-establishment in settlements cleared by spraying is unlikely. [To eradicate an endemic disease from a country at a cost of £400 is a meritorious achievement.]

R. J. Matthews

863. **II. The Treatment of Intestinal Amoebiasis with Emetine Bismuth Iodide, Glaucarubin, Dichloroacet-hydroxymethylanilide, Camoform and Various Antibiotics**

A. W. Woodruff, S. Bell, and F. D. Schofield. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **50**, 114–138, March, 1956. 12 refs.

The authors have tested, at the Hospital for Tropical Diseases, London, a series of drugs in the treatment of intestinal amoebiasis; these were the antibacterials chloramphenicol, chlortetracycline (aureomycin), and oxytetracycline (" terramycin "), the amoebicidal drugs fumagillin, " glaucarubin " (α-methyl-α-hydroxybutyric acid combined hexahydroxylactone), and " entamide " (dichloroacet-hydroxymethylanilide), the results being compared with those of emetine bismuth iodide (E.B.I.) given either alone or in combination with various other drugs. The patients, who came from " most countries of the world ", were treated in hospital.

Most of them were suffering from some form of alimentary symptoms and the majority had acquired their infection in India or tropical Africa. All drugs were given orally, and stools were examined microscopically each day during treatment, at the conclusion of treatment, and subsequently at monthly intervals for 2 or 3 months, or in some cases at longer intervals up to 4 years. In the trials of glaucarubin and entamide the faeces, in addition to microscopical examination, were examined by a modification of the formol–ether technique, a concentration technique which is said to be more efficient than the zinc sulphate method and which can be performed in 5 minutes [but details have not yet been published].

In 64 cases E.B.I. was given in a dosage of 195 mg. per day for 10 days, each dose being preceded by a sedative; only one of these cases relapsed. This drug was also given in various combinations with " diodoquin " (diiodohydroxyquinoline), carbarsone, emetine hydrochloride, and oxytetracycline. Out of 89 cases given E.B.I. plus diodoquin there were 3 relapses, and out of 43 treated with E.B.I. plus diodoquin and carbarsone there were 2 cases of relapse. No relapses occurred among 8 patients given E.B.I. plus emetine hydrochloride or 3 given E.B.I. plus oxytetracycline. Thus the addition of other drugs to the standard course of E.B.I. did not improve the results.

Two of the antibacterial drugs were ineffective: all 6 patients treated with chloramphenicol relapsed, and out of 6 given chlortetracycline, 3 relapsed. Oxytetracycline was somewhat more successful, only 2 out of 14 patients treated with 2 g. daily for 10 days relapsing. Fumagillin in doses of 60 mg. per day for 10 days (8 cases) or 14 days (24 cases) caused toxic symptoms such as dermatitis and albuminuria in 11 cases. Out of 27 cases of amoebiasis treated with this drug 3 relapsed, all 3 being among those given the longer course. " Camoform ", a new synthetic drug, was tried in 12 cases, 3 of which relapsed; the dose was 1·5 or 2·0 g. per day for 7 to 10 days. Glaucarubin, a new drug isolated from the American plant *Simarouba glauca*, was given in various dosages. The most effective dose proved to be not less than 4 mg. per kg. body weight for 10 days, since out of 28 patients given this dosage only 2 relapsed. However, signs of toxicity limited the upper dose level to 8 mg. per kg., since above this dose some patients complained of nausea; the leucocyte count was not adversely affected by the drug. Entamide, another new synthetic amoebicide, was administered in doses ranging from 2 to 21 mg. per kg. body weight per day for 10 days. Out of 17 cases given more than 12 mg. per kg. only 2 relapsed, whereas out of 23 given less than this dose, 8 relapsed. No side-effects were noted and the drug did not affect the leucocyte count.

From these results the authors conclude that emetine bismuth iodide is still the most satisfactory drug in the treatment of intestinal amoebiasis, but that glaucarubin and entamide are worth further study. (The paper is followed by an interesting discussion.) *R. A. Neal*

864. **The Treatment of Amebic Dysentery with Streptomycin–Polymyxin–Neomycin–Bacitracin Combination**

A. Z. Shafei. *Antibiotic Medicine* [*Antibiot. Med.*] **2**, 158–165, March, 1956. 14 refs.

The author reports, from the University of Alexandria, Egypt, the results of the treatment of 30 cases of symptomatic amoebiasis with a combination of dihydrostreptomycin, polymyxin, bacitracin, and neomycin (" polisinerge "), this compound being used in the hope that the antibacterial properties of streptomycin and polymyxin would potentiate the amoebicidal activity of bacitracin and neomycin. The drugs were administered in the form of capsules, each containing polymyxin B sulphate (10,000 units), dihydrostreptomycin (150 mg. base), neomycin (175 mg. base), and bacitracin (2,500 units).

Of the 30 patients, 9 had acute amoebic dysentery and the remaining 21 had suffered from recurrent dysentery over the previous one to 7 years (average 2·8 years).

In 26 cases intestinal ulceration was observed on sigmoidoscopy, the remaining 4 patients being acutely ill and considered unfit for this procedure. For the purposes of treatment the cases were divided into three equal groups of 10 (each of which included 3 of the acute cases) which received respectively the following regimens: (1) two capsules 4 times daily for 5 days; (2) one capsule 4 times daily for 10 days; and (3) two capsules 4 times daily for 5 days, followed by one capsule 4 times daily for 5 days. Faecal smears were examined twice weekly during the first 2 weeks, once weekly for the next month, and then fortnightly for 3 months; 18 (60%) of the patients were followed up for a further 3 months.

In all three groups there was prompt clearing of clinical symptoms. However, although the clinical symptoms were most rapidly relieved by the treatment given to Group 1, the relapse rate was lowest in Group 3, the number of relapses in the three groups being 3, 2, and 1 respectively.

[The author affirms that these results show that the treatment given to Group 3 was the most efficacious, but in the abstracter's opinion the number of cases in each group was too small for the difference to be statistically significant.] *R. A. Neal*

865. **Oral Streptomycin in Bacillary Dysentery**
G. SANGSTER. *Lancet* [*Lancet*] **1**, 723–725, May 19, 1956. 6 refs.

An analysis is presented of the results obtained with streptomycin by mouth in 1,474 proved cases of bacillary dysentery seen at the City Hospital for Infectious Diseases, Edinburgh, between November, 1949, and October, 1954. In 1,177 of the cases the infection was due to *Shigella sonnei* and in 297 to *Sh. flexneri*. The ages of the patients ranged from 5 days to 79 years, but most of them were under 10 years; 53 were symptomless carriers. In 4 cases death occurred within 24 hours of admission, before any specific treatment had been given. Patients under 10 years of age received 1 g. and those over 10 years 2 g. of streptomycin daily for a period of 5 days, treatment being started as soon as there was bacteriological proof of infection—that is, within 36 hours. Patients were not discharged until 3 consecutive faecal examinations, carried out during the week after treatment ceased, proved negative; for patients returning to institutions 6 negative results were required.

Of 1,138 patients under the age of 6 years, 961 (84·4%) were cured after one course of streptomycin, and of 336 over this age, 306 (91%) were cured after one course. The results varied throughout the 5-year period, the proportion of cures after one course falling by about 10% in both age groups; a second course of streptomycin, however, usually sufficed to achieve a cure in all cases. The clinical response was rapid, irrespective of the infecting organism. The number of infections due to *Sh. flexneri* increased from 5 to 25% in the 2-year period 1951–53. No toxic effects were observed, and the duration of stay in hospital was reduced [no figures are given]. There was no evidence of drug resistance [but again no figures are given].

During 1953 a sulphonamide, phthalylsulphacetamide, was tried in 102 cases of bacillary dysentery and the results compared with those obtained in a similar number of cases treated with streptomycin. Of the former group 53 were cured and of the latter 87.

[These results show once again that antibiotics are more efficacious than the sulphonamides in the treatment of dysentery. It would seem that Sonne organisms are becoming sulphonamide-resistant. There appears to be little to choose at present between streptomycin and the tetracyclines so far as results in comparable series are concerned.] *I. M. Librach*

866. **Influence of the Tuberculosis Factor on the Clinical and Immunological Evolution of Child Contacts with Leprosy Patients**
J. M. M. FERNANDEZ. *International Journal of Leprosy* [*Int. J. Leprosy*] **23**, 243–258, July–Sept., 1955 [received May, 1956]. 18 refs.

The author reports a study of the immunological relationship between leprosy and tuberculosis. Since 1939 he has observed the incidence of leprosy among 100 child contacts of relatives suffering from the disease, 83 being in contact with lepromatous leprosy and 27 with the tuberculoid form. No case of leprosy was observed among the latter group of contacts, but lesions developed in 32 of the 83 children in contact with lepromatous leprosy. The present paper is concerned particularly with the immunological features of these 83, who were therefore divided into 3 groups: (1) 28 given B.C.G. vaccine either intradermally or by mouth; (2) 32 not vaccinated with B.C.G. but who were tuberculin-positive; and (3) 23 not vaccinated with B.C.G. who were tuberculin-negative to a 1 in 10 dilution of tuberculin. In 9 of the 28 subjects in Group 1 leprosy developed, the lesions being of the tuberculoid type in 8 and indeterminate in one. In Group 2 there were 13 children with leprosy, the lesions being of the tuberculoid type in 12 and indeterminate in one. Lesions developed in 10 of the 23 children in Group 3, and were of the tuberculoid type in 5, lepromatous in 3, and indeterminate in 2. The lepromin reaction (Mitsuda) was positive in 26 cases in Group 1, 30 in Group 2, and 9 in Group 3. Although the incidence of leprosy was highest in Group 3 the difference was not statistically significant. The important finding according to the author was the high proportion of lepromatous cases in Group 3. He points out that in this group without B.C.G. vaccination but giving a positive reaction to the tuberculin skin test there is a tendency for the more malignant form of leprosy to develop, suggesting that immunity to tuberculosis, produced either spontaneously or by B.C.G. vaccination, has some protective effect in those cases in which there is subsequent infection with *Mycobacterium leprae*. *William Hughes*

867. **Clinical Aspects of Brucellosis in East Africa**
P. E. C. MANSON-BAHR. *Journal of Tropical Medicine and Hygiene* [*J. trop. Med. Hyg.*] **59**, 103–106, May, 1956. 9 refs.

Allergy

868. **Treatment of Contact Dermatitis Due to Handling Antibiotics**
R. M. MORRIS-OWEN. *British Medical Journal* [*Brit. med. J.*] **1**, 654–657, March 24, 1956. 7 refs.

The successful treatment of 6 patients (2 doctors and 4 nurses) suffering from occupational dermatitis due to sensitivity to streptomycin and penicillin by the daily injection of minute doses is reported from the Radcliffe Infirmary, Oxford. The diagnosis was confirmed by skin tests, and in this connexion the author claims that "drop testing"—that is, application of a drop of solution to the skin for 20 minutes followed by thorough washing—is as effective as patch testing and provokes less local or remote reaction. Subcutaneous injection is necessary, however, for quantitative testing to establish the treatment dose. Initial doses ranged from 0·1 unit in patients who had recently recovered from a severe reaction up to 1 unit in milder cases. This was increased gradually up to the level tolerated by the patient or the level capable of giving protection. A dosage of 1 to 2 units daily was given in mild cases and 5 to 10 units in more severe cases; one patient, however, could tolerate only 0·001 unit initially. These minute amounts prevented local or remote reactions for periods of 8 to 24 hours. Daily treatment for a few days enabled the patient to resume the handling of the antibiotic, and after a period of weeks or months of daily injections and constant handling a relatively lasting tolerance was acquired. In subjects sensitive to both antibiotics treatment for penicillin sensitivity was given first, contact with streptomycin being avoided and treatment for sensitivity to it given later. *J. Pepys*

869. **Liberation and Depletion of Histamine from Human Skin. Effect of an Antihistamine and Hydrocortisone on the Activity of the Histamine Liberator, Compound 48/80**
I. L. BERNSTEIN and S. M. FEINBERG. *Journal of Allergy* [*J. Allergy*] **27**, 231–235, May, 1956. 2 refs.

The authors have previously reported that the injection into the skin of Compound 48/80 (a condensation product of *p*-methoxyphenylethylmethylamine with formaldehyde) releases histamine and produces a weal and flare. Repeated injections deplete the local supply of histamine so that the response becomes less or absent, but the reaction to a local injection of histamine is also diminished, suggesting that Compound 48/80, in addition to depleting the histamine supply, causes some change in the tissues. In order to test the validity of these findings and to test the nature of the change in the tissue, 4 healthy subjects received daily injections of the compound at 8 skin sites on the back, sometimes preceded by the injection of tripelennamine ("pyribenzamine") or hydrocortisone. After 5 days the response to injected histamine was tested on the same sites. The diminished response to histamine in skin sites previously treated with Compound 48/80 was confirmed. Pretreatment with tripelennamine did not prevent depletion of histamine from the skin by Compound 48/80, but it did reduce the degree of refractoriness of the tissues to histamine. It is therefore assumed that this substance protects the cells from damage by Compound 48/80. Hydrocortisone, on the other hand, had little of this protective effect. *H. Herxheimer*

870. **Treatment of Hay-fever with Hydrocortisone Snuff**
H. HERXHEIMER and M. MCALLEN. *Lancet* [*Lancet*] **1**, 537–539, April 28, 1956. 6 refs.

The results obtained with hydrocortisone snuff in 24 patients with severe hay-fever are reported. None had responded adequately to antihistamine drugs, and in all of them a positive reaction to skin tests with grass pollen was obtained. The contents of a capsule containing 15 mg. of hydrocortisone acetate and 85 mg. of lactose were sprayed into the nose from an insufflator over a period of 24 hours. In some cases it was necessary first to relieve nasal blockage by vasoconstrictor drugs. Of the 24 patients, 23 obtained complete relief within 2 weeks, most of them responding dramatically within 48 hours. In 17 out of 19 followed up for the whole season symptoms were controlled, although 9 had to continue the inhalations throughout this period. After the first 5 days' treatment most of these 17 patients remained free from symptoms up to 16 days. Antihistamine drugs were taken at the same time by the 13 patients in the series who had previously obtained partial relief from them. Irritation of the eyes and conjunctival injection cleared up in 20 out of 24 patients. No chest symptoms were observed in 4 of the 10 patients with seasonal asthma. *J. Pepys*

871. **Prednisone in the Treatment of Bronchial Asthma. Comparative Study on the Effect of Cortisone and Prednisone.** [In English]
E. ANDERSSON. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] **9**, 297–303, 1955 [received April, 1956]. 8 refs.

Prednisone differs chemically from cortisone in having a double bond between the first and second carbon atoms. Clinically, it does not appear to cause sodium retention and potassium excretion, although it may give rise to ulcers of the gastro-intestinal tract. In the investigation reported in this paper from the University of Copenhagen 15 asthmatic patients, selected from a large series who were failing to obtain relief from cortisone and hydrocortisone, received prednisone in a dosage of 7·5 to 20 mg. daily. A good response was obtained in 14, of whom 9 became symptom-free. No complications were observed over a follow-up period of 3 months. When prednisone was started after a course of cortisone the patients at first lost weight, but later regained it; none complained of dyspeptic symptoms.
A. W. Frankland

Nutrition and Metabolism

872. **Preliminary Evaluation of a Non-dietary Regimen for Reducing Cholesterol Levels in the Aged**
N. BLUMBERG, M. W. FISCHBACH, and L. ZISSERMAN. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] **4**, 276–285, March, 1956. 2 figs., 19 refs.

The authors report that the oral administration of lipotropic substances for 3 months resulted in a significant lowering of the serum cholesterol level in 25 elderly patients on an unrestricted diet at the Home for the Jewish Aged, Philadelphia. The lipotropic substances —betaine (N-trimethyl glycine), choline, and inositol— were given in a " general tonic " containing 15% alcohol, caffeine, ferric iron, vitamin B_{12} (cyanocobalamin), nicotinamide, pyridoxine, and riboflavine.

[Insufficient notice is taken of the fact that in only 5 cases was the trial in any way controlled; and in one of these 5 the placebo had the same effect as the lipotropic substances. The conclusions must therefore be treated with reserve.] *P. D. Bedford*

873. **Induced Azotemia in Humans following Massive Protein and Blood Ingestion and the Mechanism of Azotemia in Gastrointestinal Hemorrhage**
T. D. COHN, M. LANE, S. ZUCKERMAN, N. MESSINGER, and A. GRIFFITH. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **231**, 394–401, April, 1956. 5 figs., 8 refs.

An investigation designed to ascertain the relative importance of protein ingestion and impaired renal function in the azotaemia accompanying gastro-intestinal haemorrhage was carried out at the Brooklyn Jewish Hospital, New York, the subjects being 5 healthy male volunteers. The blood urea nitrogen level was determined at 2- to 3-hour intervals for 11 to 14 hours and again 24 hours after ingestion of blood or protein. The 24-hour urinary nitrogen excretion was also determined, but no faecal studies were carried out. Administration of 800 ml. of whole blood (180 g. of protein), which was given by stomach tube, resulted in an increase in the blood urea nitrogen level of 4 to 7 mg. per 100 ml. (25 to 35%) above the fasting level at about 5 hours. The equivalent amount of protein hydrolysate led to a rise of 19 to 21 mg. per 100 ml. 7 to 9 hours after ingestion, a slight increase persisting at 24 hours. Beefsteak, if necessary supplemented by protein hydrolysate, also brought about a greater rise in blood urea nitrogen level than did whole blood, the rise being 14 to 45 mg. per 100 ml. above the fasting value (67 to 237%) 6 to 10 hours after ingestion. The urinary excretion of nitrogen after protein hydrolysate or meat was double that after blood, suggesting that the latter was less readily absorbed. The authors consider that the degree of azotaemia after gastrointestinal haemorrhage is related to the size of the haemorrhage, since this influences both protein ingestion and, by changes in blood volume, renal function. Nitrogen ingestion from protein in the diet may be important if there is coincidental renal disease or impaired renal function secondary to blood loss.
Kenneth Gurling

874. **Late Prognosis in Coeliac Disease**
M. K. M. LINDSAY, B. E. C. NORDIN, and A. P. NORMAN. *British Medical Journal* [*Brit. med. J.*] **1**, 14–18, Jan. 7, 1956. 1 fig., 21 refs.

Of a large group of patients suffering from coeliac disease, 37 survivors were investigated by Hardwick in 1938 (*Arch. Dis. Childh.*, 1939, **14**, 279), the oldest patient at that time being aged 16¼. In the present paper the authors report the results of a follow-up study of these patients carried out in 1953–4. Of the 26 who could be traced, one had died from tuberculosis and only written or verbal information could be obtained about a further 7, of whom 4 were reported to be in good health while 3 had had relapses requiring hospital treatment. The remaining 18 patients were seen and examined by the authors, 11 of them being investigated as in-patients at Hammersmith Hospital (Postgraduate Medical School of London).

As a group, the patients were physically and emotionally immature. The haemoglobin value was less than 90% (Haldane) in 7 cases, in 5 of which there was also evidence of iron deficiency. In the 11 patients tested for fat absorption (intake 50 g.) this was shown to be more than 90% in 10 cases and 69% in the eleventh; there was evidence of defective vitamin-A absorption in 10 cases, but the faecal nitrogen content was normal in all cases tested, while 4 out of 9 patients investigated had a flat type of glucose tolerance curve. In all 18 patients the blood pressure was within normal limits and there was no evidence of rickets or osteomalacia, either on radiography or by determination of the blood calcium, phosphorus, and alkaline-phosphatase values and by calcium infusion tests.

However, clinical examination showed that 4 of the 18 patients had not completely recovered, and laboratory investigations revealed that 4 more had some degree of malabsorption. In the 1938 study 4 of these 8 patients had been classified as recovered for more than 3 years, 2 still had active disease, and one was normal. (No information could be obtained about the eighth.) The 2 patients with active coeliac disease in 1938 were found to be normal in 1953–4. The authors conclude that coeliac disease is essentially a chronic relapsing disorder.
M. Lubran

875. **The Effect of Ventilatory Insufficiency on Respiratory Compensations in Metabolic Acidosis and Alkalosis**
J. W. POPPELL, P. VANAMEE, K. E. ROBERTS, and H. T. RANDALL. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **47**, 885–890, June, 1956. 3 figs., 2 refs.

Gastroenterology

876. **Use of Chlorpromazine in Treatment of Certain Gastrointestinal Disturbances**
L. M. Asher. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 1281–1285, April 14, 1956. 15 refs.

The results obtained with chlorpromazine in the treatment of 62 patients with various gastro-intestinal disorders in which psychosomatic factors were considered to be important are discussed in this paper from the Cedars of Lebanon Hospital, Los Angeles. The conditions most frequently diagnosed were "anxiety state with associated indigestion" (21 cases), peptic ulcer (7), and ulcerative colitis (7). The ages of the patients ranged from 18 to 78 years.

In 41 cases there was subjective improvement, which was most striking in those in which anxiety was a marked feature. Of the 7 patients with ulcerative colitis 6 failed to respond. Some unfavourable effects of the drug were observed in 30 cases, including drug sensitivity in 6; the author states, however, that in some instances symptomatic relief was obtained in spite of these reactions. *T. D. Kellock*

877. **The Etiology and Treatment of Peptic Esophagitis**
F. S. Cross and E. B. Kay. *Annals of Surgery* [*Ann. Surg.*] **143**, 360–368, March, 1956. 5 figs., 11 refs.

In this paper from Cleveland, Ohio, the authors discuss the treatment of 55 cases of oesophagitis seen over a 6-year period, 41 of which were associated with a hiatus hernia. Repair of the hernia was undertaken even when the oesophagitis was mild, and the results of this treatment were good. Conservative measures—that is, regulated diet and dilatation of the oesophagus—were employed in cases of oesophagitis without hiatus hernia. The authors state that in these cases oesophagogastrectomy is liable to be followed by further oesophagitis, and that subtotal gastrectomy, as advocated by Wangensteen, may be beneficial by providing good gastric drainage as well as by reducing secretion of acid. The value of pyloromyotomy in addition to repair of the hiatus hernia in preventing postoperative oesophagitis is discussed. *Guy Blackburn*

878. **Chronic Ulcer of the Thoracic Portion of the Oesophagus.** (О хронической язве грудного отдела пищевода)
T. A. Suvorova. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **34**, 57–62, No. 3, 1956. 5 figs., 8 refs.

The possible complications of chronic ulceration of the thoracic oesophagus are illustrated by the presentation of two cases. The first patient, a girl of 25, had had dysphagia intermittently since the age of 11. Operation eventually became necessary, and 8 cm. of the oesophagus was resected. Histological examination showed it to contain a chronic ulcer with adenocarcinomatous changes. The girl made a good recovery and when seen 13 months later was symptom-free and in much improved general health. The second patient, a man of 52 who had suffered from dysphagia for many years, was admitted to hospital as an emergency with severe haematemesis and symptoms of internal bleeding. Transfusion gave temporary relief, but was followed by further profuse and fatal haemorrhage. Necropsy revealed two chronic ulcers of the oesophagus, one of which had perforated into the aorta.

The author emphasizes the need for full investigation and supervision of such cases, and for operation without undue delay in resistant cases. *L. Firman-Edwards*

STOMACH AND DUODENUM

879. **Clinical Diagnosis of Pyloric Obstruction. The Soda-water Test**
F. Lees. *British Medical Journal* [*Brit. med. J.*] **1**, 1016–1019, May 5, 1956. 4 refs.

The diagnostic value of the soda-water test in cases of pyloric obstruction was studied at the Royal Infirmary, Sheffield. The test is carried out as follows. The patient's abdomen is examined; he then drinks a glass of soda-water in the sitting position and lies down again immediately afterwards. If no gastric bulge is seen more soda-water is given; usually 5 to 10 oz. (140 to 280 ml.) suffices to produce a stomach bulge. If peristalsis is visible the response to the test is considered to be positive; if peristalsis is absent the response is regarded as negative. A large, distended stomach without peristalsis is suspect but not positively diagnostic.

This test was performed in a large number of unselected patients before *x*-ray examination. Of 58 in whom there was radiological evidence of duodenal ulcer, 47 gave a negative response to the soda-water test and 11 gave a positive response. No radiological evidence of pyloric obstruction was found in the former group; in the latter group there were 4 cases of established pyloric stenosis, 2 other "operated cases" with active duodenal ulcer without fibrotic stenosis, and 4 cases in which there was presumed to be pylorospasm in the active phase of chronic duodenal ulceration. Of 17 cases of benign gastric ulcer, proved at *x*-ray examination or at gastroscopy, 15 in which the response to the soda-water test was negative showed no radiological evidence of pyloric obstruction; in the 2 positive cases there was partial obstruction due to active ulcers within a moderate distance of the pylorus. Positive results in the soda-water test were obtained in 9 out of 12 cases of gastric carcinoma, even in the absence of vomiting, in one case of pin-hole pylorus in which the radiological appearances were normal, and in 2 cases of duodenal obstruction due to neoplastic mass. Negative responses were obtained

in 6 patients with oesophageal lesions and in 48 with "functional dyspepsia". A false positive response was noted in only one case, diagnosed as of visceroptosis.

The author states that pyloric stenosis did not develop in any patient giving a negative response, so that no case was actually missed. In some of the positive cases the test was more valuable than *x*-ray examination in indicating the presence of pyloric obstruction.

Joseph Parness

880. **Correlation of Gross Gastroscopic Findings with Gastroscopic Biopsy in Gastritis**

L. ATKINS and E. B. BENEDICT. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 641–644, April 5, 1956. 5 figs., 13 refs.

An attempt was made at the Massachusetts General Hospital, Boston, to correlate the gastroscopic and histological appearances of the gastric mucosa in 370 patients, with special reference to gastritis. A Benedict operating gastroscope was used, and a total of 239 biopsy specimens were examined. A biopsy specimen 3 to 5 mm. in diameter provided a full thickness of the mucosa, including the muscularis mucosae.

Of 71 specimens considered to be normal at gastroscopy, 62 (87·3%) were found to be normal histologically. The gastroscopic appearances in 30 instances suggested chronic gastritis, but in 23 (76·7%) microscopical examination revealed normal mucosa. Acute gastritis was diagnosed at gastroscopy in 78 instances, but this diagnosis was confirmed histologically in only 13 (16·7%). A gastroscopic diagnosis of atrophy in 19 cases was confirmed histologically in 8, and of 41 in which both acute and chronic gastritis were diagnosed at gastroscopy normal mucosa was found in 22.

The authors conclude that the gross gastroscopic appearance of "gastritis" is not a reliable diagnostic entity and that biopsy is essential for confirmation. They consider that the term hypertrophic gastritis should be abandoned.

I. McLean Baird

881. **Hematemesis and Melena. With Special Reference to Causation and to the Factors Influencing the Mortality from Bleeding Peptic Ulcers**

F. AVERY JONES. *Gastroenterology* [*Gastroenterology*] **30**, 166–190, Feb., 1956. 1 fig., 34 refs.

The author reviews a series of 1,910 cases of haematemesis and melaena coming under his care at the Central Middlesex Hospital, London, since 1941. Of these, 1,764 were proved cases of peptic ulcer, the remainder being made up of cases of simple or malignant tumour, portal hypertension, diverticulum, neurofibroma, haemangioma, and other "unusual causes".

The "acute lesion group" consisted of 559 patients who showed no significant radiological findings 2 to 3 weeks after the haemorrhage, but in 111 out of 303 of these cases an acute gastric ulcer was demonstrated by gastroscopy. Patients in this group frequently had long but indefinite dyspeptic histories, and a short history of acute dyspepsia immediately before the haemorrhage was more common than in chronic cases; severe pain was never recorded. The mortality was very low and almost exclusively confined to patients over the age of 60. The author is definitely of the opinion that insoluble aspirin has been responsible for a number of cases of haematemesis and advocates the use of the soluble form only.

In the period 1941–6 only an occasional patient was operated on, but from then on surgical treatment was employed more frequently. The main indication for surgical intervention was chronic ulcer in patients over 40 suffering from persistent pain, recurrent bleeding, and shock. With increased use of surgery, however, the over-all mortality was not reduced, partly perhaps because more patients over 60 were included. Patients who showed a decreased mortality rate were those under 60 and those of any age with chronic gastric ulcer. The author therefore favours "continuing to maintain a surgical bias" in the management of these cases. He stresses the importance of anaesthesia being induced by an experienced anaesthetist, and also of the early introduction of a cuffed endotracheal tube to avoid the risk of inhalation of stomach contents. Follow-up studies showed that later ulcer complications were much more frequent in male patients treated medically and frequently necessitated partial gastrectomy at a later date. The author's general conclusion is that these patients "should be admitted to medical wards and the ideal professional combination is a keen physician and a somewhat reluctant surgeon".

R. Schneider

882. **Complete Nutriment for the Therapy of Peptic Ulcer**

A. WINKELSTEIN and E. SCHWEIGER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 1111–1113, March 31, 1956. 1 fig., 7 refs.

A new high-calorie nutrient, "sustagen", which is soluble in water, palatable, and contains mineral and vitamin supplements, was tried in the treatment of 30 patients with gastro-intestinal disorders at the Mount Sinai Hospital, New York, 100 g. of sustagen supplying 390 Calories—24% from protein and 8% from fat. It was found that a dose of 135 g. neutralized the gastric contents for up to 2 hours (6 patients), whereas a meal of 3 arrowroot biscuits produced considerable acid secretion (10 patients). Likewise, sustagen neutralized the acid produced by histamine (4 patients). For 2 hours after a dose of sustagen (4 patients) there was no free acid in the gastric juice, but after ingestion of 240 ml. of whole milk there was a transient decrease in free acid lasting for only half an hour, followed by considerable rebound secretion. In 6 patients the nocturnal acid secretion was completely neutralized by a continuous intragastric drip of sustagen.

These preliminary observations suggest that this nutrient may be of value in the treatment of peptic ulcer. The authors have used it in only a few cases so far, but with success.

A. Gordon Beckett

883. **The Results of Treatment of Gastric Cancer. 15 Years Experience with 201 Resections.** [In English]

O. OLSSON, A. WESTERBORN, and R. ENDRESEN. *Acta chirurgica Scandinavica* [*Acta chir. scand.*] **3**, 1–15, May 31, 1956. 5 figs., 11 refs.

LIVER

884. **Peripheral Venous Oxygen Saturation in Patients with and without Liver Disease**
E. SILVERSTEIN. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **47**, 513–518, April, 1956. 18 refs.

It has been suggested that the occurrence of palmar erythema and an increased cardiac output with proportionately small oxygen consumption in cirrhosis of the liver indicates arteriovenous shunting of blood in the skin. The author, working at the University of Minnesota Hospitals, Minneapolis, has measured the oxygen saturation of peripheral venous blood in 4 patients with hepatic cirrhosis, one with acute hepatitis, and 4 control subjects with no liver disease. All were afebrile and room temperatures were comparable. In the patients with liver disease the mean oxygen saturation of blood from the antecubital vein was high and the mean arteriovenous oxygen difference in the arm was only 0·6 volume %. If the circulation to the hand was occluded, however, antecubital venous oxygen saturation fell to normal values. On the other hand the femoral venous oxygen saturation in the patients with liver disease did not differ significantly from the control values. The results support the theory that increased arteriovenous shunting occurs in the hands of patients with liver disease. *P. C. Reynell*

885. **A Critical Study of the Blood Ammonia Level in Liver Disease.** (Étude critique de l'ammoniémie au cours des affections hépatiques)
A. VARAY, J. CROSNIER, and M. MASSON. *Archives des maladies de l'appareil digestif et des maladies de la nutrition* [*Arch. Mal. Appar. dig.*] **45**, 5–31, Jan.–Feb., 1956. 5 figs., bibliography.

In this paper from the Hôpital Necker, Paris, the authors report the results of a study of the blood ammonia content in 6 cases of severe hepatic failure with coma, 17 cases of cirrhosis with ascites, 4 cases of jaundice due to various causes, and 3 cases of other hepatic disorders, and also in 13 healthy control subjects. The metabolism of ammonia and the methods used for its measurement in the blood are reviewed, the technique of Conway being regarded as satisfactory provided the estimation is made at a standard interval (which the authors have fixed at 3 minutes) after the blood is taken.

Their findings indicate that elevation of the blood ammonia content in hepatic coma is not completely related in degree to the depth of coma, nor is it pathognomonic of the condition. An elevated blood ammonia level, for example, occurs in non-comatose decompensated cirrhotics. The authors believe that an increase in the blood ammonia content reflects a disturbance of the portal circulation and the by-passing of the liver by means of spontaneous porta-caval shunts, which allow ammonia to reach the general circulation in excess. More rarely the rise in blood ammonia level is determined by functional failure of the liver itself. The significance of these findings is fully discussed and a practical warning is given against the excessive administration of high-protein diets in cases of liver disease and the administration of ammonium chloride with mercurial diuretics in the treatment of ascites.
J. McMichael

886. **Glutamine and Ammonia in Hepatic Coma.** (Glutamine et ammonium au cours du coma hépatique)
M. V. SCHWARZMANN. *Archives des maladies de l'appareil digestif et des maladies de la nutrition* [*Arch. Mal. appar. dig.*] **45**, 32–44, Jan.–Feb., 1956. 24 refs.

An increased blood glutamine level was found in 9 out of 12 cases of hepatic coma, whereas in 20 cases of cirrhosis without coma the figures fell within the normal range. In 3 of the 9 cases of coma the blood ammonia level was determined simultaneously and was found to be increased to a similar degree. Glutamine has hitherto been regarded as the product of the detoxication of ammonia by glutamic acid, but the hypothesis that hepatic coma results from a failure of this mechanism has not been confirmed by therapeutic experience, the administration of glutamic acid having proved ineffective in the treatment of hepatic coma and causing no increase in the blood glutamine level. The metabolic problems involved in the explanation of these biochemical findings are fully discussed, but no firm conclusion is reached. *J. McMichael*

887. **Non-cirrhogenic Subacute Alcoholic Hepatitis.** (Les hépatites alcooliques subaiguës non cirrhogènes (formes histobiologiques))
G. ALBOT, C. S. SCHLUMBERGER, C. M. FAYE, J. RUFFINO, and S. RAIMBAULT. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **32**, 1705–1722, May 20, 1956. 12 figs., 38 refs.

The authors of this paper from the Hôtel-Dieu, Paris, describe the morphological and biological changes found in the subacute forms of alcoholic hepatitis, that is, in the initial stages of the process which may eventually lead to cirrhosis, but before definite cirrhotic changes have developed. They point out that cirrhosis, with its characteristic disturbance of the lobular architecture of the liver, is preceded by a state of cirrhogenic hepatitis or precirrhosis in which the hepatic lesions caused by alcoholism are already in an advanced stage, and that precirrhosis is itself preceded by subacute alcoholic hepatitis, in which the hepatic changes are still reversible.

On the basis of a study of 22 cases of this last condition by means of liver biopsy and biochemical tests they distinguish two forms of subacute alcoholic hepatitis—a cytolytic form, characterized by a generalized clarification of the cells, and a steatotic form, which is actually a cytolytic hepatitis complicated by overloading of the liver cells with fat. In both forms there are disturbances of urinary excretion, with opsiuria (fasting diuresis), galactosuria, and hippuricuria, while the results of the flocculation and "bromsulphalein" excretion tests are normal. Electrophoresis of the serum proteins shows a significant and constant reduction in the amount of α globulins present, which contrasts with slight and variable changes in the albumin, β-globulin, and γ-

globulin fractions. These findings differ from those in cirrhogenic hepatitis and cirrhosis.

Detailed reports are given of 10 cases of the cytolytic type of subacute hepatitis and 12 cases of the steatotic type. In 3 cases of the latter condition which were treated with "vagotonin" [a pancreatic extract] but without withdrawal of alcohol the steatotis disappeared, but the appearances of cytolytic hepatitis remained, and the functional disturbances were the same as before treatment. In cases of the cytolytic type of subacute hepatitis the authors obtained some functional improvement with a low-protein diet, vitamin supplements (including vitamin B_{12}), total liver extract, rest, and withdrawal of alcohol. In grave and neglected cases on the other hand they observed the development of mixed parenchymatous and mesenchymatous hepatitis, the next stage in the cirrhogenic process, characterized by abnormalities of the flocculation reactions without reduction of bromsulphalein excretion. *E. Forrai*

888. **Occlusive Hepatic Venous Catheterization in the Study of the Normal Liver, Cirrhosis of the Liver and Noncirrhotic Portal Hypertension**

W. J. TAYLOR and J. D. MYERS. *Circulation* [*Circulation (N.Y.)*] **13**, 368–380, March, 1956. 3 figs., 40 refs.

In experiments performed at Duke University, Durham, N. Carolina, on cats and human subjects a catheter introduced into a systemic vein was passed through the right atrium into the right hepatic vein under fluoroscopic control, and then onwards as far as possible under moderate pressure until its end became wedged in a small hepatic vein. In cats it was found that the pressure recorded from this catheter was essentially the same as in the portal vein. In each of 27 patients with cirrhosis this pressure (the "wedged hepatic venous pressure") was higher than in any of 18 healthy control subjects, but in 11 patients in whom the portal venous pressure was raised by some form of pre-hepatic venous obstruction the readings were normal. The wedged hepatic venous pressure was particularly high in cirrhosis with jaundice or oesophageal varices, but the degree of elevation could not be correlated with the presence or absence of ascites. *J. McMichael*

889. **Structural Alterations in the Clinical Evaluation of Cirrhosis**

F. SCHAFFNER, H. POPPER, and M. D. TORRE. *Gastroenterology* [*Gastroenterology*] **30**, 357–372, March, 1956. 6 figs., 34 refs.

The authors propose a system of classification for the evaluation of cases of hepatic cirrhosis which is based on the extent, degree, and rate of progression of the structural alterations in the liver as seen in biopsy specimens. A total of 229 biopsies were performed with the Vim–Silverman or Terry aspiration needle on 185 patients at the Cook County Hospital, Chicago, and the findings correlated with the clinical and laboratory findings. A full description is given of the histological criteria used, which were chiefly concerned with the amount of liver cell destruction and evidence of regeneration present. [The amount of fibrosis is barely mentioned, which is quite a novelty in a description of cirrhosis.]

The cirrhosis was classified as "minimal" in extent in 61 specimens, "moderately advanced" in 70, and "far advanced" in 98, specimens in each of these categories being further classified as "arrested" or "progressing" and as showing "slight" or "marked" liver cell degeneration. [For details of the methods of classification used and the distribution of the cases in each category the original paper must be consulted. A good series of photomicrographs is provided.] As the cirrhosis progressed from "moderately" to "far advanced" the incidence of splenomegaly increased from 29 to 53% and that of oedema from 34 to 54%. Jaundice did not appear to be related to the extent of the cirrhosis, but was increased in incidence in the presence of marked cell degeneration, as also were gastro-intestinal haemorrhage and abnormal results in the liver function tests. Active progression of the disease was noted in 194 biopsies, very rapid advance (florid cirrhosis) in 16, and arrest in 19; 24 of the patients died in hospital.

While admitting that a classification of cirrhosis based on morphological criteria "does not show a perfect correlation with clinical and laboratory findings" [a criticism with which the abstracter would agree], the authors claim that liver biopsy, repeated when required, is useful not only for diagnostic purposes, but also for the evaluation of the cirrhotic process for prognostic and therapeutic purposes. *J. W. McNee*

890. **The Neuropsychiatric Syndrome Associated with Hepatic Cirrhosis and an Extensive Portal Collateral Circulation**

W. H. J. SUMMERSKILL, E. A. DAVIDSON, S. SHERLOCK, and R. E. STEINER. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **25**, 245–266, April, 1956. 8 figs., 47 refs.

Patients with chronic liver disease may present a neuropsychiatric syndrome which is often misdiagnosed. In this paper from the Postgraduate Medical School of London the diagnosis and the clinical features in 17 cases are discussed. The patients, whose ages ranged from 22 to 68 years, had been ill for 6 months to 6 years, and in 8 liver disease had not been suspected.

The clinical picture was very variable. The psychiatric features were those of a chronic toxic psychosis. All stages of clouded consciousness were seen, from twilight states to delirium and coma. Mood might be euphoric, hypomanic, depressed, or paranoid, orientation for time, place, and person was disturbed, and memory for recent events was poor. An unusual combination of neurological symptoms was often found—namely, muscle rigidity, ankle clonus, and flexor plantar responses. A "flapping" tremor of the arms, an expressionless face, and a vacant stare were common, and speech and writing were disturbed. The electroencephalogram showed a slowing of the dominant rhythm from the alpha to the delta and theta ranges.

Splenomegaly was a constant finding. In 15 cases in the present series an extensive portal–systemic collateral circulation was demonstrated by percutaneous trans-

splenic venography. In 5 patients the results of liver function tests were almost normal, and the diagnosis of hepatic cirrhosis had to be confirmed by needle biopsy of the liver. The blood ammonia levels in the peripheral veins were usually raised.

Assessment of nitrogen tolerance was the most specific diagnostic procedure. A high-protein diet or administration of ammonium chloride or DL-methionine aggravated the condition. Restriction of dietary protein resulted in clinical improvement, which was considered excellent in 6 patients. The authors state that 5 patients have been on a low-protein diet for 12 to 18 months without deterioration in general health. *F. K. Taylor*

891. **Management of Patients with Portal Hypertension Undergoing Venous-shunt Surgery**
W. C. EBELING, J. P. BUNKER, D. S. ELLIS, A. B. FRENCH, F. R. LINTON, and C. M. JONES. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 141–148, Jan. 26, 1956. 7 refs.

A report is presented of experience gained over a recent 10-year period at Massachusetts General Hospital (Harvard Medical School), Boston, in the management of 129 patients subjected to porta-caval or spleno-renal anastomosis for the relief of portal hypertension. There were 104 operations on 100 patients with cirrhosis and intrahepatic portal-bed block and 36 operations on 29 patients with extrahepatic block but without evidence of cirrhosis. It is of interest that the authors did not always find it possible to distinguish these two types of case by the results of various liver function tests.

Preoperative preparation of the patients included, particularly, correction of anaemia and institution of an adequate diet—that is, of a high-carbohydrate, medium-protein diet, supplemented by vitamin-B complex and vitamin K. Most of the operations were performed under ether or cyclopropane anaesthesia; in the more recent cases spinal analgesia with procaine or tetracaine (amethocaine) was used. After operation L-glutamic acid was given by mouth or sodium glutamate by intravenous injection to reduce the high blood ammonia level, particularly in patients with incipient liver failure.

After 71 of the operations recovery was uneventful and after 38 there were serious but not fatal complications; in 4 cases death was due to complications not directly related to the liver. In 27 instances complications or death were directly related to the liver; in 22 of these frank liver failure developed, proving fatal in 8; 5 patients died from uncontrollable haemorrhage at operation. The incidence of complications and the death rate were directly proportional to the degree of liver damage as assessed by the results of liver function tests performed before operation, the prognosis being particularly poor in patients with a low serum albumin level, ascites, or jaundice. In patients with severe liver disease the death rate and the incidence of complications were higher after a porta-caval than after a spleno-renal shunt.

[This is an authoritative review of the practical factors in the management of these patients and should be read by all interested surgeons.] *F. B. Cockett*

892. **Intrahepatic Obstructive Jaundice (Primary Cholestasis), a Clinicopathologic Syndrome of Varied Etiology: a Review with Observations of the Use of Corticotropin as a Diagnostic Tool**
H. C. JOHNSON and J. P. DOENGES. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 589–616, April, 1956. 2 figs., bibliography.

Intrahepatic cholestasis is characterized by obstructive jaundice, although no obstructive agent can be found. The findings on needle biopsy of the liver may not help in diagnosis because the picture is often that of extrahepatic obstructive jaundice. Bile accumulations are present in parenchymal and Kupffer cells, and frequently there is an inflammatory-cell infiltration of the portal tracts. Extreme parenchymal-cell changes are absent. Clinically, the condition is similar to viral hepatitis, but usually the patients are less ill than those with a similar degree of jaundice and viral hepatitis. The course and prognosis are very variable; the jaundice often lasts for several months and the long-term outcome of the condition has not been adequately studied.

In this paper from the U.S. Army Hospital, Fort Jackson, South Carolina, 2 cases of intrahepatic obstructive jaundice due to viral infection are described. In one, the results of tests of parenchymal function, with the exception of the cholesterol: cholesterol-ester ratio, were normal. After 25 days of progressively increasing jaundice laparotomy was performed, but no reason for obstruction was found. A biliary catheter was left in position. During the first 24 hours after operation 30 ml. of bile was obtained. Intravenous administration of ACTH was then started, and after 2 days 350 to 490 ml. of dark clear bile was collected daily. On the ninth day following operation ACTH therapy was replaced by oral administration of cortisone, which was continued for 9 months. Convalescence was uneventful. In the second case the course was similar, but laparotomy was not performed. The response to ACTH therapy was good, and by the fourth day of this treatment the serum bilirubin level had fallen from 26 to 16·3 mg. per 100 ml.

[This excellent paper merits study in the original.] *W. H. Horner Andrews*

INTESTINES

893. **A Clinical, Physiologic and Biochemical Study of Patients with Malignant Carcinoid (Argentaffinoma)**
A. SJOERDSMA, H. WEISSBACH, and S. UDENFRIEND. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 520–532, April, 1956. 4 figs., bibliography.

Many of the clinical features of the syndrome of argentaffinoma of the small intestine associated with hepatic metastases have been ascribed to the pharmacological action of 5-hydroxytryptamine (5-HT), which is secreted in excess by the tumour mass.

The authors report, from the National Institutes of Health, Bethesda, Maryland, a detailed clinical and biochemical study of 4 patients with the syndrome, with certain biochemical findings in the urine of 2 further patients. All had flushing attacks of varying severity,

accompanied by hypotension and chronic diarrhoea, and in some by cyanosis (2 cases), bronchospasm (3 cases), and involvement of the pulmonary and tricuspid valves (3 cases). The presence of arthritic symptoms suggested the possibility of a more generalized connective-tissue disorder than one affecting the valves and endocardium only.

The blood 5-HT levels, estimated chemically, ranged from 0·5 to 2·7 μg. per ml. (normal 0·1 to 0·3 μg. per ml.). Chemical analysis showed a concentration of 0·8 mg. of 5-HT per g. of tumour tissue. Urinary excretion of the 5-HT metabolite, 5-hydroxyindoleacetic acid, ranged from 76 to 580 mg. per 24 hours (normal 2 to 9 mg. per 24 hours), measurement of the rise in this value providing the basis for a simple and rapid biochemical diagnosis of the condition. Two unidentified 5-hydroxyindoles were also detected chromatographically in the urine. Metabolic balance tests and tracer studies using tryptophan labelled with radioactive carbon confirmed that up to 60% of tryptophan was diverted from the production of nicotinic acid and protein to the 5-hydroxyindole pathway, compared with about 1% in normal subjects. Relative tryptophan deficiency, it is suggested, may thus be a contributory factor in the pathogenesis of the syndrome.

Treatment of 2 of the patients with lysergic acid diethylamide caused aggravation of the flushing attacks and bronchospasm, although the reverse might have been expected because of the known action of the drug *in vitro* as an antagonist of 5-hydroxytryptamine.

M. Sandler

894. **Ulcerative Colitis and Pregnancy**

B. B. Crohn, H. Yarnis, E. B. Crohn, R. I. Walter, and L. J. Gabrilove. *Gastroenterology* [*Gastroenterology*] **30**, 391–403, March, 1956. 1 fig., 16 refs.

In order to verify a clinical impression that pregnancy exerts a deleterious effect on chronic ulcerative colitis of the indeterminate sort the authors, working at the Mount Sinai Hospital, New York, have analysed the records of 110 women with a history of ulcerative colitis who had had, in all, 150 pregnancies; the patients were divided into four groups, following the classification of Abramson *et al.*

In Group 1, consisting of women who became pregnant when their colitis was quiescent, there were 47 women with 74 pregnancies. Of these, 32 (44·4%) were uneventful but 40 (55·5%) were accompanied by a recurrence of the colitis. The majority of these relapses (20 out of 32) occurred during the first trimester of pregnancy, while the next highest incidence was during the postpartum period, particularly between 2 and 6 weeks after delivery. In this group there were 6 spontaneous abortions, 5 therapeutic abortions (which led to recovery from the colitis), and one stillbirth.

In Group 2, consisting of 25 patients who had active colitis at the time of conception, there were 38 pregnancies, of which 9 (24%) were uneventful, but 29 (76%) were accompanied by deterioration of the colitis. Again the majority (12 out of 16) deteriorated in the first trimester and the others in the postpartum period; there were 4 spontaneous abortions, one therapeutic abortion, and 2 stillbirths in this group.

Group 3 contained 19 patients in whom the disease started *de novo* during pregnancy, in the majority during the first trimester. In 13 cases the colitis was severe, ending fatally in one. In 4 cases the colitis remitted shortly after delivery, but in 11 it continued to be severe for a prolonged period. Of the 4 patients in this group who had further pregnancies, all suffered a relapse of the colitis. In all cases in Group 4 the pregnancy was uneventful, the colitis starting only in the postpartum period.

Thus in about half of the cases of colitis deterioration occurred during pregnancy—of which, nevertheless, there is a reasonable probability of a normal outcome. The decision to perform therapeutic abortion must be made in the first 3 months of pregnancy, but each case must be judged individually, particular attention being paid to whether the pregnancy is wanted or not. Most cases can be carried through to delivery with the usual precautionary measures, particularly administration of corticotrophin, which has no harmful effect on the pregnancy. The authors advise their patients with active colitis (who have a 76% risk of deterioration in pregnancy) to avoid pregnancy until the disease is quiescent. As regards patients in Group 3 (colitis starting *de novo* during pregnancy) the illness may run a severe and sometimes fatal course, and here the authors consider that therapeutic abortion is very frequently indicated. They comment that women who had had corrective surgical procedures for their ulcerative colitis tolerated pregnancy uneventfully, and point out in conclusion that although it is tempting to associate the changes in the colitis during pregnancy with variations in the endocrine secretions, no investigation of this possibility has yet been made.

A. Gordon Beckett

895. **Experiences with Prefrontal Lobotomy for Intractable Ulcerative Colitis**

R. W. Levy, H. Wilkins, J. D. Herrmann, A. C. Lisle, and A. Rix. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 1277–1280, April 14, 1956. 4 figs., 9 refs.

Prefrontal lobotomy was carried out at University Hospital, Oklahoma, on 5 patients in whom varying degrees of obsessive-compulsive behaviour, deep-steated hostility, and periods of depression were associated with severe and long-standing ulcerative colitis. All the patients were extremely ill, their poor physical condition precluding colectomy. In one case intestinal obstruction developed, followed by perforation of the colon and death one week after the operation. In 4 cases there was striking improvement, the number of stools decreasing and the fever subsiding within one week. Relapse occurred in one case four months after discharge and colectomy was performed. Three patients were well 5½, 1½, and one year after operation respectively. In one case there was a marked improvement in the radiological appearances of the colon. In all the cases the mental symptoms responded very satisfactorily to the operation.

T. D. Kellock

Cardiovascular System

896. **Surgical Treatment of Portal Hypertension. Results in 64 Cases**
A. I. S. MACPHERSON, J. A. OWEN, and J. INNES. *Lancet* [*Lancet*] **1**, 353–357, April 7, 1956. 13 refs.

In this paper the authors review the progress of 64 cases of portal hypertension treated surgically at the Edinburgh Royal Infirmary during the 8 years up to the end of 1953 and make an attempt to assess the value of such treatment. The operations performed on these patients totalled 68 and were as follows: porta-caval anastomosis, 7; splenectomy and spleno-renal anastomosis, 19; splenectomy alone, 27; limited oesophagogastrectomy, 8; ligation of the splenic artery, 4; other operations, 3.

In general, the recurrence of bleeding after operation was as variable and unpredictable as with medical treatment. Only after limited oesophagogastrectomy has there been no recurrence of haemorrhage, but the maximum follow-up period in this group is only 2 years. There was no evidence of deterioration of liver function as a result of operation, whether portal blood was deviated from the liver or not. The correction of the leucopenia and thrombocytopenia which follows splenectomy (but not other procedures) was confirmed, and shown to persist up to 5 years after operation. Comparison of the survival rates in this series and in similar reported series treated medically showed the former to be slightly, but for the most part not significantly, better.

[The authors point out that it is difficult to assess the value of surgery in this condition owing to the composite nature of the disorder. In this series the difficulty is unfortunately increased by the fact that no fewer than 6 different types of operation were employed, some of which are now known to be unsatisfactory, and the comparison of such a mixed series with cases treated medically elsewhere can hardly lead to any useful conclusions. The paper does, however, present interesting material and illustrates the problem of the statistical treatment of this subject.] *F. B. Cockett*

897. **Fluorescent Patterns of Intracutaneous Wheals in Normal and Edematous Extremities**
R. W. GIFFORD, J. H. WINDESHEIM, J. E. ESTES, and G. M. ROTH. *Circulation* [*Circulation* (*N.Y.*)] **13**, 515–523, April, 1956. 4 figs., 9 refs.

A method for demonstrating cutaneous lymphatic capillaries by injecting a fluorescent dye (riboflavin) intradermally is described. The patterns observed in the skin under ultra-violet light after such injections are classified as types 0 to 4, the former indicating no demonstration of lymphatic capillaries while the latter indicates maximal demonstration. Patterns of type 4 were not seen in normal extremities and only 1·5% of the injections into normal extremities resulted in patterns of type 3. In contrast, 17% of the injections into extremities with lymphedema showed patterns of type 4 and 44% showed patterns of type 3.

Patterns of types 3 and 4 were observed much less frequently in extremities with edema owing to causes other than lymphedema. Only in nephrotic edema did the frequency of patterns of types 3 and 4 (25%) approach that seen in lymphedema.

Certain of the data presented indicate that extensive filling of the lymphatic capillaries (as in types 3 and 4) indicates lymphatic incompetency and not just lymphatic distention. However, further observations are necessary before the value of the fluorescent wheal test in the differential diagnosis of peripheral edema can be definitely determined.—[Authors' summary.]

898. **Effect of Pregnancy on the Course of Heart Disease. Re-evaluation of 106 Cardiac Patients Three to Five Years after Pregnancy**
M. M. MILLER and J. METCALFE. *Circulation* [*Circulation* (*N.Y.*)] **13**, 481–488, April, 1956. 12 refs.

A follow-up study of 106 women with heart disease who were seen during pregnancy at the Boston Lying-in Hospital 3 to 5 years previously is reported. There were no maternal deaths during pregnancy or the puerperium, but 3 patients in whom pregnancy was terminated died 6 months, 3 years, and 4 years respectively afterwards. Functional capacity in the remaining 103 was assessed according to the American Heart Association Classification. This revealed no change in 65 and an improvement in 27 (cardiac surgery had been performed in 6 of the latter group); the condition of 11 patients had deteriorated. Several explanations for the relatively benign course in 92 patients suffering from rheumatic heart disease are suggested. It is emphasized that the improvement in functional ability may have been due in large part to the fact that the first assessment was made during pregnancy. However, a lower functional capacity was found in only 3 out of 9 patients who were pregnant at the time of the follow-up examination. No permanent change in the degree of heart disease could be attributed directly to pregnancy. *R. S. Stevens*

899. **Disposable Membrane Oxygenator (Heart–Lung Machine) and its Use in Experimental Surgery**
W. J. KOLFF, D. B. EFFLER, L. K. GROVES, G. PEEREBROOM, and P. P. MORACA. *Cleveland Clinic Quarterly* [*Cleveland Clin. Quart.*] **23**, 69–97, April, 1956. 15 figs., 23 refs.

This paper describes the development at the Cleveland Clinic, Cleveland, Ohio, of a relatively simple and inexpensive heart–lung machine with a low rate of flow and reports its successful use in over 130 perfusion experiments upon dogs.

Extracorporeal oxygenation of vena caval blood is effected by circulating it through a "lung unit" con-

sisting of two flat polythene tubes 2 inches (5 cm.) wide and with walls 1/1,000 inch (0·025 mm.) thick placed between strips of plastic-covered "fiberglas" sheeting 7 m. long which are then rolled round a can and the whole enclosed in a plastic bag. The blood passes through the flat tubes by means of inlet and outlet tubes, and oxygen at 30 litres a minute is fed into the base of the bag, being expelled with carbon dioxide from the loosely tied top.

The complete apparatus contains 500 ml. of blood and has a total oxygenating area of 14,000 sq. cm., being able to achieve between 95 and 98% oxygen saturation in 75 ml. of blood per minute. By using a number of these units in parallel the apparatus is adaptable for perfusion operations on animals of 2 and 21 kg. body weight.

Details of the circuit, the constant-volume pumping system, and the operative technique are given, while experimental observations concerning haemolysis, acidosis, changes in the serum potassium:sodium ratio and body temperature, the dangers of "heparin rebound", clotting disturbances, and electrocardiographic changes are reported and discussed. *C. A. Jackson*

900. **Elective Cardiac Arrest by the Melrose Technic. Potassium Asystole for Experimental Cardiac Surgery**
W. J. KOLFF, D. B. EFFLER, L. K. GROVES, G. PEEREBROOM, S. AOYAMA, and F. M. SONES. *Cleveland Clinic Quarterly* [*Cleveland Clin. Quart.*] **23**, 98–104, April, 1956. 2 figs., 4 refs.

The observation of Melrose *et al.* (*Lancet*, 1955, **2**, 21) that a temporary state of cardiac arrest can be achieved in dogs by injecting 25% potassium citrate solution mixed with blood directly into the clamped aorta has been confirmed by the authors. In 10 dogs whose circulation was maintained by means of the Kolff heart–lung machine [see Abstract 899] effective potassium asystole was maintained for periods ranging from 30 seconds to 23 minutes, with ultimate restoration of normal rhythm upon removal of the occluding clamp and a flushing out of the coronary circulation. Administration of calcium chloride was not required, and a dangerous rise in the serum potassium level was not observed. *C. A. Jackson*

901. **Elective Cardiac Arrest in Open-heart Surgery. Report of Three Cases**
D. B. EFFLER, L. K. GROVES, F. M. SONES, and W. J. KOLFF. *Cleveland Clinic Quarterly* [*Cleveland Clin. Quart.*] **23**, 105–114, April, 1956. 3 figs., 3 refs.

Employing the Kolff oxygenator [see Abstract 899] and the Melrose technique of cardiac arrest [see Abstract 900], the authors carried out successful operations on the open heart for closure of interventricular defects in 3 children aged 17 months, 4 years, and 3 years respectively. The duration of asystole ranged from 7½ to 13 minutes. Normal rhythm occurred spontaneously in each case, but one child died from unexplained causes 10 hours after operation. (The successful use of this technique in 5 additional cases is noted in an addendum.) *C. A. Jackson*

DIAGNOSTIC METHODS

902. **The Bronchoscopic Measurement of Left Atrial Pressures**
J. HUTCHISON, T. D. V. LAWRIE, and R. M. THOMSON. *Scottish Medical Journal* [*Scot. med. J.*] **1**, 139–147, April, 1956. 5 figs., 9 refs.

In assessing the suitability for valvotomy of patients with mitral stenosis a knowledge of the left atrial blood pressure would be useful. Further, a direct pressure recording may be of more value than an estimate of pulmonary hypertension obtained by wedging a cardiac catheter in the pulmonary artery. The bifurcation of the trachea is a direct posterior relation of the left atrium; A needle introduced through the carina or anteromedial wall of either main bronchus near the mid-line should enter the left atrium. In 65 cases of mitral stenosis at the Royal Infirmary, Glasgow, a needle with a side aperture was so introduced through a bronchoscope after premedication with pethidine. The needle was connected by a polythene tube to a manometer, and a sterile heparinized saline drip entered the system. Of the 65 punctures, 60 were successful, the chief cause of failure being the entrance of the needle into the pulmonary artery. Tachycardia, which developed in many of the cases, was one of the major difficulties in recording satisfactory tracings. There appears to be no great danger in the procedure. The pressure tracing obtained is reproduced and analysed. The results of this method are probably more accurate than those of cardiac catheterization since there is less chance of damping and distortion. However, the cardiac catheter gives, in addition, pressure recordings from the right side of the heart and permits calculation of cardiac output.

In the authors' view the results do not warrant use of the method as a routine. They state that a new approach for left atrial puncture described by Bjork *et al.* (*Ann. Surg.*, 1953, **138**, 718), which allows the recording of pressures from the left atrium, left ventricle, and aorta, may be of greater value in the diagnosis and assessment of mitral- and aortic-valve lesions. *D. Goldman*

CONGENITAL HEART DISEASE

903. **Corrected Transposition of the Great Vessels**
B. S. CARDELL. *British Heart Journal* [*Brit. Heart J.*] **18**, 186–192, April, 1956. 3 figs., 29 refs.

In this communication from King's College Hospital Medical School, London, the author analyses the various possible combinations of inversion of the atria, ventricles, or great vessels (that is, placement of the structures concerned on the wrong side) and of transposition of the great vessels (that is, anterior placement of the aorta and posterior placement of the pulmonary artery, with origin from the wrong ventricles). It is possible for transposition of the great vessels to be "corrected" naturally and not to cause cyanosis if the ventricles supplying them are themselves wrongly placed.

He then describes a case of this rare developmental anomaly in a female infant aged 3½ months, not normally

cyanosed, with 2:1 A-V heart block, who died in an attack of cyanosis 20 minutes after admission to hospital. The atria were normally placed, but the right atrium opened by a biscupid valve into an anterior ventricle morphologically resembling the mirror image of a left ventricle, and in turn gave rise to a posteriorly placed pulmonary artery. The left atrium emptied by a tricuspid valve into a ventricle resembling the mirror image of a right ventricle, and gave rise to an anteriorly placed aorta. Interventricular septal defects were also present. The coronary arteries arose from the posterior and right anterior aortic sinuses. The records of the 24 other published examples of corrected transposition of the great vessels are briefly reviewed. *J. A. Cosh*

904. **Patent Ductus Arteriosus with Pulmonary Hypertension. An Analysis of Cases Treated Surgically**
F. H. Ellis, J. W. Kirklin, J. A. Callahan, and E. H. Wood. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **31**, 268–285, March, 1956. 6 figs., bibliography.

Since there is a good deal of uncertainty regarding the selection for surgical treatment of patients with patent ductus arteriosus (P.D.A.) associated with pulmonary hypertension the present analysis was carried out at the Mayo Foundation, Rochester, Minnesota, in the hope of clarifying the position, a total of 72 reported cases of P.D.A. with pulmonary hypertension being first reviewed. In this series operative closure of the ductus carried an over-all mortality of 18% (13 deaths), but in the 16 patients with a right-to-left shunt the rate was 56% (9 deaths), haemorrhage from the ductus or pulmonary artery during operation being a major cause.

The authors then consider in some detail 30 out of 272 cases of P.D.A. operated on at the Mayo Clinic up to April, 1955; of this total, 45 had pulmonary hypertension, but the discussion is restricted to the 30 in which cardiac catheterization before operation showed a pulmonary arterial pressure higher than 60 mm. Hg. The ages of the patients ranged from 2½ months to 59 years, but half of them were under 15 years. Coexistent lesions present were aortic coarctation (4 cases), atrial septal defect (2), and ventricular septal defect (2). A right-to-left shunt was demonstrated in 14 cases, and had undoubtedly been present at some time in several others. Simultaneous determination in the radial and femoral arteries of oxygen saturation values and the plotting of "arterial indicator-dilution curves" were found to be of great value in demonstrating the size of the shunt. Of the 30 patients, 5 died as a result of operation (mortality 17%) and there were 2 later deaths; all the deaths occurred in patients with a right-to-left shunt, representing a mortality of 50% in this type of case. Of the 23 survivors, 20 are well, one has paraplegia due to prolonged operative clamping of the aorta because of haemorrhage, one patient (aged 59) has mild heart failure controlled by digitalis, and one has been lost sight of. Recanalization occurred in 3 patients, 2 of whom are well and the other has subsequently died. A satisfactory reduction in pulmonary arterial pressure was noted in 9 out of 12 patients in whom closure of the ductus was successful, as shown by re-catheterization in the postoperative period. This satisfactory response included 3 cases in which a right-to-left shunt had been demonstrated before operation.

The authors conclude that all cases of P.D.A. with left-to-right shunt should be treated by operation, but that closure should not be carried out in those with a predominantly right-to-left shunt, or in those in whom the pulmonary arterial pressure rises and the systemic pressure falls when the ductus is occluded on the operating table. Patients with P.D.A. resulting in pulmonary hypertension usually have a short, wide ductus; the ligation of such a ductus is unsatisfactory, the recurrence rate being high, and division is the only method to ensure success. It is emphasized that in such cases the pulmonary artery is large, thin-walled, and friable and as it is thus easily damaged its wall should not be included in the clamp. Hypothermia was employed in one such case, and the extra time which its use conferred for cross-clamping of the aorta above and below the ductus while the ductus was being divided and sutured added greatly to the ease and safety of the operation.
F. J. Sambrook Gowar

905. **Ventricular Septal Defects with Pulmonary Hypertension**
J. W. DuShane, J. W. Kirklin, R. T. Patrick, D. E. Donald, H. R. Terry, H. B. Burchell, and E. H. Wood. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 950–953, March 17, 1956. 7 figs., 10 refs.

The authors report, from the Mayo Clinic, the results in 20 cases of ventricular septal defect, in 3 of which the defect was closed by direct suture and in 17 by insertion, at open cardiotomy, of a non-absorbable polyvinyl-sponge prosthesis. The patients, one a man aged 29 and the 19 others children under the age of 12, were variously handicapped by low exercise tolerance and showed tumultuous heart action, a systolic thrill, a long, harsh, systolic murmur at the left lower border of the sternum, and increased pulmonary vascular pulsation visible on screening. Preoperative cardiac catheterization indicated large arterio-venous shunts and, in most cases, pulmonary arterial pressures close to the peripheral arterial pressure.

During operation the circulation was maintained by a Gibbon-type pump-oxygenator, blood being collected from the venae cavae and coronary sinus and returned, oxygenated, to the left subclavian artery, this procedure allowing the heart to be opened for periods up to 45 minutes. There were 4 postoperative deaths, 3 being among the first 7 cases but only one among the next 13; the cause of death was pulmonary complications, associated in one case with complete atrio-ventricular dissociation. Interference with the conduction mechanism occurred in 9 cases, 6 showing right bundle-branch block. The presence of left ventricular hypertrophy as well as right ventricular hypertrophy gave a more favourable prognosis. The 16 survivors have shown marked clinical improvement, with increased exercise tolerance and loss of the arterio-venous shunt.
J. Robertson Sinton

906. **Auscultatory and Phonocardiographic Signs of Atrial Septal Defect**
A. LEATHAM and I. GRAY. *British Heart Journal* [*Brit. Heart J.*] **18**, 193–208, April, 1956. 13 figs., 22 refs.

This detailed report from the Institute of Cardiology, London, is based upon the phonocardiographic recordings made from 40 cases of atrial septal defect which were confirmed by cardiac catheterization. In 7 of the 40 there was, in addition, stenosis of the pulmonary valve and in 10 pulmonary hypertension. Auscultation showed that the first heart sound was loud in 17 cases, possibly because of accentuated tricuspid valve closure; it was also widely split in the 6 cases of total right bundle-branch block, the mitral element preceding the tricuspid. Splitting of the second sound was wide in 35 cases, and usually recognizable by ear, aortic preceding pulmonary valve closure. This splitting was thought to be due to a prolonged right ventricular ejection time and late pulmonary valve closure rather than to electrical delay in right ventricular activation. In 3 patients in whom the defect was closed surgically splitting of the second sound was abolished, although partial right bundle-branch block remained.

In all the cases there was a systolic murmur in the pulmonary area which was of greatest intensity at the moment of maximum right ventricular ejection, diminishing and ceasing before closure of the pulmonary valve; this phenomenon was considered to be due to increased ejection through the pulmonary valve. In 7 cases a thrill accompanied the murmur, and in 4 of these there was associated pulmonary valve stenosis. Diastolic murmurs were present in 27 cases and were of two types. In 7 the long, high-pitched murmur was characteristic of pulmonary regurgitation, but in 21 it was of short duration, of slightly delayed start in diastole, was best heard to the left of the lower sternum, and was thought to arise from the greatly increased flow through the tricuspid valve. *J. A. Cosh*

907. **Atrial Septal Defect**
L. DEXTER. *British Heart Journal* [*Brit. Heart J.*] **18**, 209–225, April, 1956. 9 figs., 47 refs.

In this paper the author reviews 60 cases of atrial septal defect investigated by cardiac catheterization at the Peter Bent Brigham Hospital, Boston. The shunt of blood from the left atrium into the right generally occurs with a negligible pressure difference between the atria (the difference with a normal septum being about 5 mm. Hg). The shunt must therefore be attributed to the greater distensibility of the right ventricle in diastole, which allows it to accept all of the right atrial blood as well as some from the left atrium. A small cross-shunt from right atrium into left ventricle may also occur, and this explains the slightly lowered systemic arterial blood oxygen saturation sometimes found. In 11 of the 60 cases this was below 90%, these patients having a low right ventricular output and thus a less distensible right ventricle in diastole. There was no evidence, however, that the arterial oxygen unsaturation was due to impaired oxygenation of the blood in the lungs.

Diminished right ventricular output was closely related to increased pulmonary vascular resistance, which was found in 31 of the 67 studies made (catheterization was performed twice in 7 cases), in 18 instances being more than double the normal. Significantly increased pulmonary vascular resistance was not met with in patients under 20 years of age, and did not necessarily occur in patients over 40. In 3 of the 7 patients reinvestigated after a few years' interval pulmonary resistance had risen. The author believes an increased resistance to be an acquired rather than a congenital feature in such cases. How much the occurrence of thrombosis in the pulmonary arteries may contribute to this is not known.

The two ventricles appear to differ in the mode of their failure when this occurs. Right ventricular failure is most likely in the face of a raised pulmonary arterial pressure, but does not necessarily set up raised atrial pressures as a result; ineffective right ventricular filling in diastole then causes a reversal of the shunt, accompanied by cyanosis. Left ventricular failure seems to occur in the face of relatively trivial additional lesions, such as mitral incompetence; it leads to raised atrial pressures, which, however, does not necessarily have the effect of increasing right ventricular output.

Severe mitral stenosis in combination with atrial septal defect (Lutembacher's syndrome) is difficult to detect, for dilatation of the left atrium does not occur. This condition was diagnosed in 2 cases on the finding of a pressure difference between the left atrium and ventricle in diastole; both these patients were much improved after valvotomy. Some cases of atrial septal defect with congestive heart failure may mimic mitral stenosis, giving rise to rumbling in mid-diastolic murmurs with presystolic accentuation and opening snaps. Closure of the defect was attempted in 7 such patients, but 5 of them died. *J. A. Cosh*

CHRONIC VALVULAR DISEASE

908. **Angiocardiographic Observations of Intracardiac Flow in the Normal and in Mitral Stenosis**
L. A. SOLOFF, J. ZATUCHNI, H. M. STAUFFER, and E. W. KELLY. *Circulation* [*Circulation* (*N.Y.*)] **13**, 334–350, March, 1956. 5 figs., 10 refs.

The intracardiac flow of a radio-opaque medium injected intravenously was studied by means of simultaneous biplane angiography at the Temple University and Episcopal Hospitals, Philadelphia, in 4 healthy subjects, in 22 patients with mitral stenosis not treated surgically, and in 31 patients after mitral valvotomy for mitral stenosis. Exposures (about 80 in number in each case) were made at 0·7-second intervals in the postero-anterior and left lateral projections simultaneously during the passage of the medium through the heart, and the duration and degree of opacification of each vessel and chamber was determined.

In mitral stenosis there was a disproportionate prolongation of the time taken by the medium to pass through the pulmonary artery and left atrium; the amount of delay in the left atrium gave no clue to the

practical problem of whether the stenosis was or was not accompanied by mitral regurgitation. Valvotomy did not alter the general pattern, and since gross delay in the left atrium may also occur in other forms of severe heart disease the angiocardiographic appearances in mitral stenosis are of no diagnostic value.

[Fine judgment is needed to extract detailed information from such pictures; for example, the moment of "earliest opacification" depends very much on subjective factors.] *J. McMichael*

909. **The Pattern of Respiration in Rheumatic Heart Disease**

R. J. SHEPHARD and A. VENNER. *British Heart Journal* [*Brit. Heart J.*] **18**, 241–247, April, 1956. 1 fig., 26 refs.

The pattern of respiration was examined at Guy's Hospital, London, in 116 patients with rheumatic valvular heart disease—55 with pure mitral stenosis and the remaining 61 with other valvular lesions—measurements being made, both at rest and after standard pedalling exercise, of the respiratory minute volume, respiratory rate, tidal volume, expiratory reserve, and pulmonary arterial and capillary pressures. The resting vital capacity and expiratory reserve were considerably reduced in both groups. The increase in respiratory rate with exercise was almost double that of normal subjects, and this gives a useful indication of the degree of pulmonary congestion; at the same time, however, respiration became mechanically less efficient. The symptom of dyspnoea seemed to be associated primarily with the reduction in vital capacity, although there was no clear correlation between the latter and the degree of disability or the pulmonary vascular pressures.

The conclusion is reached that in the assessment by laboratory methods of the symptom of dyspnoea, account should be taken both of the reduction of vital capacity and of the loss of respiratory efficiency.

A. Schott

ENDOCARDITIS

910. **Phenoxymethyl Penicillin (Penicillin V) Therapy of Subacute Bacterial Endocarditis**

E. L. QUINN, J. M. COLVILLE, F. COX, and J. TRUANT. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 931–936, March 17, 1956. 6 figs., 15 refs.

After satisfying themselves that phenoxymethylpenicillin ("penicillin V") taken by mouth produced a satisfactory blood concentration of the antibiotic the authors gave oral doses of 2,000,000 units every 4 hours day and night up to 6 weeks in the treatment at the Henry Ford Hospital, Detroit, of 4 patients with subacute bacterial endocarditis. Two patients in whom the infection was due to *Streptococcus viridans* have remained well for 4 and 3 months respectively after cessation of treatment. A third, in whom *Neisseria sicca* was the infecting organism, required injections of streptomycin to produce bacteriological remission. The fourth patient, who was found to be suffering from infection due to *Staphylococcus albus*, relapsed despite the addition of streptomycin but improved again on administration of chloramphenicol, streptomycin, and erythromycin.

The authors conclude that phenoxymethyl penicillin may prove adequate for infections due to penicillin-sensitive organisms such as *Str. viridans*, but that in the absence of a positive culture of this organism it cannot be relied upon in such conditions as bacterial endocarditis. *J. Robertson Sinton*

911. **Subacute Bacterial Endocarditis. Splenectomy in Cases Refractory to Antibiotic Therapy**

C. J. LINGEMAN, E. B. SMITH, J. S. BATTERSBY, and R. H. BEHNKE. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **97**, 309–314, March, 1956. 8 figs., 6 refs.

With antibiotic therapy alone 60 to 70% of cases of subacute bacterial endocarditis are cured. Antibiotic therapy may fail, however, because the spleen acts as a focus of reinfection, discharging organisms from an infected infarct or abscess into the blood stream. Three cases are described from the Indiana University Medical Center, Indianapolis, in which appropriate antibiotic therapy failed to secure a remission. Pain in the splenic area or a palpable spleen led to splenectomy, and in each case an infected infarct was found. Further antibiotic therapy resulted in complete remission of the disease. *James W. Brown*

DISTURBANCES OF RHYTHM AND CONDUCTION

912. **The Significance of the Intensity and Time of Appearance of the Korotkoff Sounds in Auricular Fibrillation**

W. RODBARD and J. MARGOLIS. *Circulation* [*Circulation (N.Y.)*] **13**, 510–514, April, 1956. 4 figs., 4 refs.

Simultaneous recording of the sounds at the brachial artery and of the electrocardiogram in 7 patients with auricular fibrillation provided a basis for satisfactory estimation of the mean systolic and mean diastolic blood pressure levels. To obtain these values, the rate of occurrence of brachial sounds at a mean arterial pressure to apical beats is first determined. Higher or lower cuff pressures at which this rate is reduced to about 50% are then used to determine the mean systolic and diastolic pressures respectively. The time of the sounds and their intensities and durations are related to the duration of the preceding cardiac cycle and to a factor dependent on the blood pressure and the compression produced by the cuff.

For very short preceding cycles, no Korotkoff sound is heard or recorded. With longer preceding cycles, sounds are heard. The time from the Q wave of the electrocardiogram to the onset of the sound is shortened as the preceding cycle is more prolonged. This suggests that the transmission time of the pressure pulse wave in the arterial tree may be related to the stroke output. The intensity and duration of the sound, at least at mean arterial pressure levels, is also associated with the duration of the previous cycle, and presumably with the stroke output.—[Authors' summary.]

913. **Termination of Ventricular Fibrillation in Man by Externally Applied Electric Countershock**
P. M. Zoll, A. J. Linenthal, W. Gibson, M. H. Paul, and L. R. Norman. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 727–732, April 19, 1956. 6 figs., 13 refs.

The authors report that ventricular fibrillation which occurred in 4 elderly patients at Beth Israel Hospital, Boston (respectively due to acute myocardial infarction, the rapid injection of procainamide for rapid arrhythmia, and intoxication with digitoxin, and in the course of a Stokes–Adams attack), was terminated successfully on 11 occasions by means of an electric countershock applied to the chest wall. Three of the patients died, but the fourth made a complete recovery; in the fatal cases death was attributed mainly to delay in applying the treatment, the circulation having been ineffective for 7 minutes or more before defibrillation, whereas in the survivor treatment was applied within about 3 minutes of the onset of fibrillation.

The defibrillator used had a variable transformer permitting conversion of the current from 120 volts to a range of 0 to 720 volts. The duration of the current was fixed at 0·15 second by a suitable condenser in a rotary circuit. The step-up transformer and the power relay contacts were capable of transferring approximately 12,000 watts (15 amperes at 720 volts) for 0·15 second at 1-second intervals, the current being transmitted to the precordial region by two copper electrodes 7·5 cm. in diameter. When ventricular standstill followed defibrillation an external cardiac pacemaker was used to restart cardiac rhythm. The authors conclude that, in spite of the potentially dangerous voltages used, external electrical countershock with this apparatus is a safe and (if immediately applied) an effective procedure.

H. E. Holling

CORONARY DISEASE AND MYOCARDIAL INFARCTION

914. **Painless Cardiac Infarction**
W. Evans and G. C. Sutton. *British Heart Journal* [*Brit. Heart J.*] **18**, 259–272, April, 1956. 9 figs., 38 refs.

During a period of 5 years 70 patients (56 men and 14 women) with cardiac infarction were seen at the London Hospital and in private practice who had suffered no pain or even discomfort associated with the attack. In 26 cases the infarction was restricted and was found fortuitously, being diagnosed from the presence of certain electrocardiographic features which are described in detail. In 21 cases auricular arrhythmia was present, and in 16 hypertension (with sinus rhythm in 9, and with auricular fibrillation in 7). Examples are quoted from the literature to show the wide discrepancies between the figures given by different authorities for the incidence of painless cardiac infarction, and the reasons for these differences are discussed. In many cases the reason for the absence of pain remains obscure. In the authors' largest group (restricted infarction) it is assumed to be related to the slowness of the infarction.

A. Schott

915. **Serum Aminopherase (Transaminase) in Diagnosis of Acute Myocardial Infarction**
A. A. Kattus, R. Watanabe, C. Semenson, W. Drell, and C. Agress. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 16–20, Jan. 7, 1956. 3 figs., 5 refs.

Preliminary observations having indicated that the serum transaminase level might be of diagnostic value in myocardial infarction, the authors, at the University of California Medical Center, Los Angeles, estimated this level in 11 healthy subjects, 22 patients not suspected of having acute myocardial infarction or liver disease, 4 with liver disease, 14 with proved myocardial infarction, and 24 with anginal pain. In the 11 healthy subjects the serum transaminase level ranged from 16 to 24 (average 20) units, while in the group of 22 patients not thought to have myocardial infarction the level ranged from 11 to 42 (average 20·5) units. A figure of 40 units was therefore taken as the upper limit of the normal range.

In 13 out of 14 patients with myocardial infarction the serum transaminase level was high. Serial estimations showed that the level did not rise until 6 to 12 hours after infarction, that the peak level occurred less than 36 hours afterwards, and that in most cases the level returned to normal by the fifth day. An increase in the serum transaminase level was observed in 4 out of 24 patients with angina pectoris but without evidence of myocardial infarction, in 3 with hepatitis, and in one patient with hepatic cirrhosis. In hepatitis the peak level was reached in 13 to 18 days, the level becoming normal in 32 to 33 days.

Robert de Mowbray

916. **Myocardial Infarction: Changing Sex Ratio and other Factors**
Kyu Taik Lee and W. A. Thomas. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **97**, 421–430, April, 1956. 4 figs., 17 refs.

To provide additional data on the epidemiological aspects of myocardial infarction an analysis was made of all necropsies performed on adults between 1910 and 1954 at Barnes Hospital, St. Louis, a large general hospital serving all economic classes. In 500 out of the total of 8,183 examinations acute myocardial infarction was a principal diagnosis, the incidence rising from 0·5% during the period 1910–19 to 10·2% in 1945–54. Possible relationships between this increase, which affected all age groups, and such factors as the accuracy of diagnosis and the consumption of tobacco and fats are discussed. The authors note especially that the ratio of the incidence of myocardial infarction among males to that among females in this series fell from approximately 2:1 for the period 1910–39 to 1·1:1 for 1940–54, the ratio for the whole period being 1·2:1. This contrasts sharply with the difference in incidence between the two sexes as judged on clinical grounds, the ratio of the frequency of the clinical diagnosis of myocardial infarction among males to that among females in the authors' hospital during an 8-year period being 2·4:1, and ranging from 3:1 to 7:1 in reports from other sources. The incidence of myocardial infarction rose steadily with the age in

females, while in males it was highest at 60–80 years and fell after the age of 80. The incidence was lower in negroes than in white subjects in this series, but did not appear to be significantly related to the patient's social and economic status; yet the clinical diagnosis in the same hospital was more common among fee-paying patients. The incidence of diabetes mellitus was higher in cases of acute myocardial infarction than in the other subjects.

[It must be assumed that only a proportion of the patients who died in the hospital came to necropsy, and there are certain features, such as the low average age (males 54, females 42) in the necropsy series and the wide discrepancy between the sex distribution in this series and in hospital admissions for the same period, which point to selection. Unless the factors which determine selection for necropsy can be stated, the significance of incidence rates in such a series as this must be open to question.] *J. N. Agate*

917. Relationship of Coronary Heart Disease to Respiratory Disability. Investigation of a Random Sample of Coal-workers Aged 55–64 from a Mining Valley in South Wales

T. E. COTES, I. T. T. HIGGINS, and A. J. THOMAS. *British Medical Journal* [*Brit. med. J.*] **1**, 601–603, March 17, 1956. 1 fig., 20 refs.

During 1955–6 a random sample of 47 men aged 55 to 64, drawn from a group of 1,160 miners and ex-miners living in the Rhondda Fach, South Wales, were examined to ascertain the incidence of coronary arterial disease, and whether or not this was associated with pulmonary disability, as is the case in bronchitis and pneumoconiosis —conditions which might be expected to co-exist in a group of this age. Coronary heart disease, both clinically active and silent, was found in 18 of the men (38%). Bronchitis was diagnosed in 16 (34%), all of whom had productive cough apart from intermittent acute attacks, and 2 had pulmonary heart disease. Pneumoconiosis of varying degrees of severity was present in 28 men, 11 (23%) had progressive massive fibrosis (P.M.F.), and one of these had pulmonary heart disease. The authors state that the incidence of bronchitis and pneumoconiosis corresponds to that found in other random groups of similar age and may be accepted as representative. Of the 18 men with coronary heart disease, 5 had co-existing bronchitis and 3 had P.M.F.; of 29 without coronary disease, 11 had bronchitis and 8 P.M.F., the remaining 10 men having none of the three diseases. Comparison of these figures with those calculated from the over-all incidence on a proportional basis did not suggest any relationship between the three conditions.

Respiratory function was assessed subjectively (in accordance with Fletcher's grading for breathlessness) and also objectively, the maximum voluntary ventilation (M.V.V.) being estimated by the indirect method. A significant relationship was found between the two, the M.V.V. decreasing by 17·07 (±2·247) litres per minute for " unit drop in clinical grade of breathlessness ". The average values for M.V.V. were as follows: (1) in 15 out of 29 subjects with no coronary heart disease but with bronchitis or P.M.F., 65·8 litres per minute; (2) in 8 out of 18 with coronary disease and co-existing bronchitis or P.M.F., 76·1 litres per minute; (3) in 10 men with coronary disease alone, 91·2 litres per minute. Thus the highest values were found in men with coronary disease but no pulmonary disorder, while the lowest values were in those with bronchitis. This lessened ventilatory disability in those with coronary arterial disease was not due to age and is attributed to " differences of temperament and body type ". Exercise tolerance tests showed no appreciable variation in the mean ventilation figure of 26·5 litres per minute for the three conditions, and the blood lactic acid response in those with coronary arterial disease was similar to that in the other groups with the same grade of clinical disability The authors conclude that in the absence of clinical manifestations of coronary arterial disease this lesion does not contribute to impaired respiratory function, but actually appears to be a favourable factor in those prone to develop symptoms of breathlessness.
V. Reade

918. A Controlled Study of the Effect of Intermittent Heparin Therapy on the Course of Human Coronary Atherosclerosis

H. ENGELBERG, R. KUHN, and M. STEINMAN. *Circulation* [*Circulation* (*N.Y.*)] **13**, 489–498, April, 1956. 40 refs.

The effect of prolonged, intermittent administration of heparin on patients who had had an attack of myocardial infarction more than 3 months before was studied at the Cedars of Lebanon Hospital, Los Angeles. Over 200 such patients and a few with angina of effort in whom the electrocardiogram was abnormal were divided into two comparable groups, one of which received 200 mg. of concentrated aqueous solution of heparin subcutaneously twice a week and the other isotonic saline injections in a similar manner. The progress of the underlying atherosclerotic process was assessed from such factors as death from cardiovascular disease, recurrence of cardiac infarction, gangrene of a limb necessitating amputation, and cerebral vascular accidents, excluding those occurring during the first month of treatment.

Over a period of 2 years there were 18 non-fatal recurrences and 21 deaths from cardiovascular disease in the control group, compared with 5 non-fatal recurrences and 4 deaths from heart disease in the heparin-treated group, the difference being statistically significant ($p = <0{\cdot}01$). Symptomatic improvement was also noted in the heparin-treated group. In the course of over 17,000 injections of heparin there were only 3 instances of major haemorrhage, 2 being associated with underlying disease. Treatment was discontinued in only 4 cases. Protamine sulphate by intravenous injection was effective in three episodes of haemorrhage. The authors found that determination of the clotting time was not necessary. Heparin was not given to patients with severe liver disease, but was not withheld from those with duodenal ulcer, hypertension, or haemorrhoids.

Lipoprotein values were determined in a few cases only, but from these it appears that in a minority of patients

there is a sustained reduction in the average level of low-density lipoproteins, while in the majority there is only a temporary decrease following each injection. The results were considered to depend on this effect and on the physiological role of heparin in the serum-transport phase of fat metabolism rather than on intermittent anticoagulation. *R. S. Stevens*

919. **The Selection of Cases of Coronary Heart Disease Suitable for Surgical Treatment**
N. A. ANTONIUS, R. MILLER, A. D. CRECCA, and L. G. MASSARELLI. *Diseases of the Chest* [*Dis. Chest*] **29**, 305–313, March, 1956. 9 refs.

In the light of their experience of 32 operations for the relief of coronary arterial disease, carried out at St. Michael's Hospital, Newark, New Jersey, the authors discuss the selection of suitable cases and the indications for this procedure. They found the Beck Type-I operation safest; of 18 patients treated by this method (that is, the creation of pericardial adhesions), good results were obtained in 17. Among the 14 patients treated by other operations there were 3 operative deaths.

The main indication for surgical intervention is persistent angina, of " stabilized " severity and frequency. [The importance of the duration of this symptom is not discussed.] More severe symptoms—for example, angina of decubitus—may suggest that the heart condition is too far advanced for operation to be safe, while angina of quickly increasing severity and frequency is a symptom of impending myocardial infarction, and again surgery is dangerous. They recommend that in no case should operation be considered within 6 months of myocardial infarction, in order to allow time for the natural development of a coronary collateral circulation. In their opinion hypertension is not a contraindication to operation unless it is accompanied by severe arterial disease. Aortic stenosis, cardiac arrhythmia, and A–V heart block (but not bundle-branch block) are held to be contraindications to surgery. *J. A. Cosh*

HEART FAILURE

920. **Studies on the Control of Hypertension**
H. M. PERRY and H. A. SCHROEDER. *Circulation* [*Circulation (N.Y.)*] **13**, 528–536, April, 1956. 1 fig., 8 refs.

An analysis of the results of treating 114 hypertensive patients with a combination of oral hexamethonium chloride and hydrallazine at Barnes Hospital (Washington University School of Medicine), St. Louis, showed that if the dose of hypotensive drugs was adequate to restore the blood pressure to within normal limits the amount of drug required to maintain the normotensive state diminished with time. The series consisted of all patients treated with these drugs over 3 years for whom adequate daily follow-up data were available for at least one year (but excluding patients transferred to treatment with newer hypotensive drugs). All the patients had an initial average diastolic pressure of over 100 mm. Hg.

After one year of therapy 79 patients whose blood pressure was effectively controlled required only an average of 73% of their initial dose of hexamethonium, whereas the other 35 patients in whom adequate control was not achieved still required 97% of the initial dose. At the end of 2 years the percentages of the initial dose in these two groups were 57 and 99 respectively. Eventually 10 of the 114 patients, including 2 whose initial diastolic pressure before treatment was between 130 and 180 mm. Hg, were gradually able to discontinue treatment and yet remain normotensive. The authors conclude that adequate and continuous drug therapy is apparently associated with a change in the basic process producing hypertension. *P. Hugh-Jones*

921. **Acetazolamide (Diamox) in the Treatment of Congestive Heart-failure**
T. HANLEY and M. M. PLATTS. *Lancet* [*Lancet*] **1**, 357–359, April 7, 1956. 4 figs., 10 refs.

The diuretic effect of the carbonic anhydrase inhibitor acetazolamide (" diamox ") on 30 patients with heart disease of varying aetiology was studied at the University of Sheffield.

Of 18 patients with congestive heart failure who were given 0·2 g. of acetazolamide 2-hourly, the intake of water and salt being kept constant, only in 3 was there a moderately good diuresis, the response in the remainder being small or negligible. In 15 cases the diuretic effects of mersalyl and acetazolamide were compared, each patient receiving 3 to 10 days' treatment alternately with acetazolamide (0·25 to 1 g. daily or on alternate days) and mersalyl (2 ml. every other day). In the group as a whole the volume of diuresis after mersalyl was almost double that after acetazolamide. Five patients showed no response at all to acetazolamide, while 2 patients who responded well to acetazolamide had an exceptionally good diuresis after receiving mersalyl. Oedema and venous congestion developed in 5 of 12 ambulatory patients who were given daily doses of 250 to 750 mg. of acetazolamide to prevent a recurrence of congestive heart failure, the other patients remaining free from symptoms during an average period of treatment of 8 months.

In all 30 patients, including those who initially showed a good diuretic response to acetazolamide, each successive dose produced progressively less effect. No significant toxic effects of acetazolamide were observed even after prolonged administration. *Gerald R. Graham*

922. **Peripheral Venoconstriction in Human Congestive Heart Failure**
J. E. WOOD, J. LITTER, and R. W. WILKINS. *Circulation* [*Circulation (N.Y.)*] **13**, 524–527, April, 1956. 2 figs., 8 refs.

In this paper from the Evans Memorial Hospital, Boston, the authors describe a method of measuring venous " tone " in human subjects by means of a water-filled, variable-depth, limb-segment plethysmograph 16·5 cm. in length which is used in combination with arterial and venous occluding cuffs. It is stated that this isolates the peripheral venous system from the influence of central venous pressure changes. They showed that the peripheral veins of patients with congestive cardiac failure were constricted, as measured by

the venous distensibility, compared with normal subjects. The procedure is described in detail.

In a study of 20 patients with heart disease and 10 control subjects it was found that the distensibility of the peripheral veins (expressed in ml. per 100 ml. of forearm tissue) in patients with congestive failure and raised venous pressure averaged 2·9±0·6 ml., compared with an average of 4·4 ml. both in patients with heart disease without failure and in the control group with no cardiovascular disease (S.D.±0·9 and 0·4 ml. respectively). The venous constriction in those with heart failure appeared to be independent of the height of the venous pressure, but in 5 of the cases studied it disappeared after successful therapy. It was established that the amount of venoconstriction (that is, decreased distensibility as compared with the normal range) could be roughly correlated with the degree of cardiac decompensation. *P. Hugh-Jones*

BLOOD VESSELS

923. **The Serum Lipids in Human Atherosclerosis. An Interim Report**

J. C. Paterson, B. R. Cornish, and E. C. Armstrong. *Circulation* [*Circulation* (*N.Y.*)] **13**, 224–234, Feb., 1956. 1 fig., 14 refs.

This is an interim report on a study of serum lipids in relation to the progression of atherosclerosis which is being made on 800 patients permanently confined to the Westminster Hospital, Department of Veterans' Affairs, Western Ontario, 700 of them being psychotic and the remaining 100 being elderly and in need of domiciliary care. Since April, 1953, specimens of blood have been obtained at yearly intervals from each patient. A portion of the serum is used immediately for estimation of its lipoprotein content in the ultracentrifuge; the remainder is fast-frozen and will be kept in the frozen state until the patient dies and necropsy has been completed, when its cholesterol and phospholipid content will be determined.

The findings are now reported in the first 50 fatalities in the series, the mean antemortem serum cholesterol and phospholipid values and those of four classes of lipoproteins (S_f 0–12, 12–20, 20–100, and 100–400) being compared statistically with the degree of atherosclerosis present at necropsy. This last was determined in segments of the coronary arteries, the basilar artery and circle of Willis, the abdominal aorta, and the left femoral artery, the degree of atherosclerosis being graded in each case as "severe", "moderate", or "slight" according to each of 6 different indices—crude morphological grading, thickness of the largest plaque, total content and concentration of lipid, and total content and concentration of calcium. Thus the relationship of each of the 6 different measures of atherosclerosis in 4 types of artery to the mean antemortem level of 6 different lipids in the serum could be determined. The calcium content of the cerebral arteries, however, was too small for its relationship to the lipid levels to be assessed, so that the number of individual comparisons totalled 138 instead of 144. Almost all the 50 subjects were in the 6th to 9th decade, the age distribution in the whole series being 40 to 90 years or more.

In the analysis of the findings in these first 50 cases only 4 of the 138 sets of comparisons showed a significant relationship, namely, an increase in the serum cholesterol: phospholipid (C:P) ratio and an increased concentration of S_f 0–12 lipoproteins in the serum in association with severe coronary sclerosis, an increased serum concentration of S_f 0–12 lipoproteins in association with severe aortic sclerosis, and an increased serum C:P ratio in association with severe femoral sclerosis. Even these associations were not consistent. In the 5 cases with the slightest and the 5 cases with the most severe apparent degree of atheroma in the aorta the serum lipid levels were not related to the degree of atherosclerosis. There was no significant elevation of the serum level of any of the lipids or lipoproteins in any of the cases with gross clinical manifestations of atherosclerosis such as coronary thrombosis. The serum cholesterol, phospholipid, and S_f 0–12 lipoprotein values estimated serially were remarkably constant in each case, but the values for the other lipoproteins were more variable. The severity of atherosclerosis in different arteries in the same individual varied widely.

The authors admit that their material was selected in that it was derived predominantly from psychotic individuals, and also that no method of assessment of the severity of atherosclerosis is entirely satisfactory. Moreover, the investigation has not been in progress for a sufficient length of time for any firm conclusions to be drawn from this preliminary survey. However, their findings so far disagree sharply with those of other workers who have correlated serum lipid and lipoprotein levels with the clinical manifestations of atherosclerosis. It is hoped to continue the study for a total period of at least 10 years. *Robert de Mowbray*

924. **A Clinical Study of a Geriatric Drug Causing a Reduction in the Blood Cholesterol Content.** (Etude clinique d'un médicament gériatrique à action hypocholestérolémiante)

G. Garrone and C. Bossoney. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **86**, 417–421, April 21, 1956. 4 figs., 39 refs.

At the Bel-Air Psychiatric Clinic of the University of Geneva 35 patients suffering from cerebral arteriosclerosis were treated with a preparation intended for administration over long periods to geriatric patients and consisting of dragees containing 0·2 g. of phenylethylacetamide together with unspecified amounts of vitamin-B complex, ascorbic acid, rutin, crataegus, and cascara sagrada. Phenylethylacetamide is stated to reduce the serum cholesterol level in animals and in man.

All the patients were over 65, and in all of them the serum cholesterol level was above 210 mg. per 100 ml. They were divided into three groups, which received 3, 4, and 6 dragees daily respectively. The duration of the trial was 5 months.

No attempt was made to assess the effect of the treatment on the clinical condition of the patients (though

their body weight, blood count, and capillary resistance were recorded and were found to be unchanged at the end of the investigation), the main object of the study being to evaluate its effect on the blood lipid levels. In most cases after the first month of treatment there was a reduction of the serum cholesterol level by an average of about 25%, which then remained fairly constant. There was a corresponding change in the cholesterol: phospholipid ratio. The electrophoretic pattern of the serum proteins showed a diminution in the albumin and an increase in the globulin, especially the beta-globulin fractions during the trial period. No unpleasant side-effects were noticed.

[The claim that phenylethylacetamide consistently reduces the serum cholesterol level has not been uniformly confirmed.] *Z. A. Leitner*

925. **Changes in the Blood Pressure following Resection of Coarctation of the Aortic Arch**
T. B. COUNIHAN. *Clinical Science* [*Clin. Sci.*] **15**, 149–159, 1956. 6 figs., 15 refs.

926. **The Temporary Thrombotic State. Application of this Concept to the Therapy of Recurrent Thromboembolism, with Bacteriologic and Roentgenologic Considerations in the Differential Diagnosis of Pulmonary Infarction and Pneumonia**
S. WESSLER, S. COHEN, and F. G. FLEISCHNER. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 413–419, March 1, 1956. 1 fig., 27 refs.

Occasionally a patient is seen with massive pulmonary infarction but in whom no evident source of emboli or recognized cause for local thrombosis can be found. The authors state that in such cases the concept of the temporary thrombotic state may be helpful; this is based on experimental and clinical data, since there is as yet no reliable clinical or laboratory test for the detection of the incipient or actively thrombotic state. Intravascular clotting is initiated by a state of hypercoagulability which may be due either to known or to as yet undefined alterations in one or more of the specific clotting factors. Among the known alterations are those concerning the convertin complex, platelet adhesiveness, and the liberation of thromboplastic elements from the gravid uterus, traumatized tissues, or a necrotic tumour. During this abnormal state, thrombosis can be initiated by minimal venous stasis that would not, by itself, result in thrombus formation. In patients showing idiopathic intravascular clotting, hypercoagulability and vascular stasis may be systemic or local, and transient, prolonged, or recurrent. The main part of this paper from Beth Israel Hospital (Harvard Medical School), Boston, is devoted to the differential diagnosis between pulmonary infarction and pneumonia, and the different bacteriological and clinical features, including the radiological and electrocardiographic findings, which distinguish pulmonary infarction from pneumonia are described, together with a typical case report. The authors advocate that anticoagulant therapy be started as soon as the diagnosis of thrombo-embolic disease has been established. *A. I. Suchett-Kaye*

PULMONARY CIRCULATION

927. **Total Anomalous Pulmonary Return. An Analysis of Thirty Cases**
V. L. GOTT, R. G. LESTER, C. W. LILLEHEI, and R. L. VARCO. *Circulation* [*Circulation (N.Y.)*] **13**, 543–552, April, 1956. 11 figs., 19 refs.

The authors present a detailed analysis of 30 cases of total anomalous pulmonary venous return to the heart in infants. In 23 cases the diagnosis was confirmed at necropsy, in 3 at operation, and in 4 cases it was accepted after thorough clinical evaluation; 17 patients were male and 13 female. Of the 23 cases examined post mortem, 13 were found to have associated patent foramen ovale, 4 patent foramen ovale together with patent ductus arteriosus, and 6 had multiple major defects. Most of the patients failed to survive the first 3 months of life, but the 7 still living are all past infancy and one is a 33-year-old woman with 2 children.

The 2 oldest patients, now aged 16 and 33 respectively, were found to have systolic pressure gradients between right ventricle and pulmonary artery of 40 and 63 mm. Hg. These patients are thought to have had pulmonary stenosis and it is postulated that this added lesion may have retarded the onset of damaging pulmonary vascular obliterative changes. Pulmonary venous drainage was into the left innominate vein and thence to a right superior vena cava (a route mistakenly called " persistent left superior vena cava " by some authors) in 7 cases, into the coronary sinus in 4, into the right atrium in 4, the inferior vena cava in 2, the right superior vena cava in 2, and into the portal vein, the coronary sinus and left innominate vein, the inferior vena cava and left innominate vein, the abdominal visceral veins, and the anterior cardinal veins in one case each; in 2 cases the route of drainage was not fully demonstrated. Cardiac catheterization, performed in 13 cases, showed the striking feature of high oxygen saturation in the right atrium, this being equal to or higher than that in the systemic arterial blood. Pulmonary hypertension was common, as also was electrocardiographic evidence of right ventricular hypertrophy; only one patient had right bundle-branch block. On radiological examination only 3 cases showed the well-known " figure-of-eight " appearance formed by the engorged superior vena cava and the heart; in the postero-anterior position 12 showed a square-shaped heart, due to massive enlargement of right atrium and right ventricle, which the authors consider to be characteristic. There was increased pulmonary vascularity, which became very marked after the first few months of infancy.

In 3 recent angiograms the following typical appearances were noted: (1) dilution of the opaque medium by a jet of non-opacified pulmonary venous blood entering the superior or inferior vena cava; (2) filling of the small left atrium immediately after opacification of a very large right atrium; and (3) simultaneous opacification of an abnormally large pulmonary artery and hypoplastic aorta. Of the 6 patients subjected to surgery, 3 survived partial or totally corrective procedures. *K. G. Lowe*

SYSTEMIC CIRCULATORY DISORDERS

928. **Diagnosis of Tumours of the Carotid Body.** (О диагностике опухолей каротидной железы)
P. P. ALEKSEEV. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **34**, 62–67, No. 3, 1956. 2 figs., 12 refs.

Tumours of the carotid body are usually non-malignant, but may give rise to incapacitating symptoms, especially in the cardiovascular system. Two cases are described in which the presence of a tumour in the side of the neck, mobile in the horizontal direction but not vertically or on deglutition, was associated with bradycardia, low blood pressure, and in one case with supraclavicular pain and Horner's syndrome. Electrical stimulation of the tumour caused a fall in arterial pressure which lasted for 40 to 60 minutes, after which the pressure gradually resumed its previous level.

Operation revealed a tumour of the carotid body, which in the case with Horner's syndrome was described as a phaeochromocytoma and in the other as a paraganglioma with evidence of malignant change. After extirpation of the tumour there was hypertension for 6 to 8 months, the blood pressure then falling to normal levels. This may be attributed to cessation of the depressor mechanism of the aortic and carotid reflexogenic zone owing to denervation of the carotid artery during removal of the tumour, or sometimes to section of the vagus nerve, as happened in the first of these two cases.

L. Firman-Edwards

929. **Observations on Angina Pectoris during Drug Treatment of Hypertension**
W. E. JUDSON, W. HOLLANDER, and R. W. WILKINS. *Circulation* [*Circulation (N.Y.)*] **13**, 553–561, April, 1956. 6 figs., 3 refs.

In view of their observation that anginal pain may occasionally be precipitated by the use of hypotensive drugs the authors present, from the Massachusetts Memorial Hospitals, Boston, the results of an experimental study of the mechanism of this therapeutic complication in which 17 patients (7 men and 10 women aged 40 to 65) with hypertensive cardiovascular or coronary arterial disease were investigated. After performing a two-step exercise test requiring 40 steps in 3 minutes 16 of the patients showed abnormalities in the electrocardiogram and 13 simultaneously complained of anginal pain. After a rest of at least 24 hours the patients were again studied before and after the intravenous injection of hydrallazine or hexamethonium, or both, a continuous recording of arterial pressure from an indwelling needle in the brachial artery and a concurrent electrocardiogram being obtained. All 17 patients experienced chest pain after the administration of hydrallazine and showed accompanying changes in the electrocardiogram, with depression of the S–T segment, similar to those seen in patients with angina of effort. Hexamethonium did not block these anginal effects of hydrallazine, which were not always associated with a fall in blood pressure and still occurred when the pressure was maintained with noradrenaline.

The authors conclude that the major factor in the production of "coronary insufficiency" (angina) after the administration of hydrallazine is an increased cardiac output associated with a rise in pulse rate, rather than a fall in blood pressure causing lowering of the aortic perfusion pressure of the coronary arteries. In contrast, the angina occurring after hexamethonium results primarily from a reduction in coronary arterial perfusion pressure during the severe hypotension, especially postural hypotension, which this drug produces. They suggest that the severity and duration of the reactions to intravenous hydrallazine appear to preclude its use as a test for coronary arterial disease.

P. Hugh-Jones

930. **Treatment of Hypertensive Emergencies: Parenteral Use of Reserpine**
R. W. GRIFFIN, J. W. STOVER, and R. V. FORD. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 593–598, March 29, 1956. 1 fig., 7 refs.

The effect of intramuscular injection of reserpine in cases of sustained severe hypertension (200 to 270 mm. Hg systolic and 110 to 166 mm. Hg diastolic in the supine position) was studied at the Veterans Administration Hospital and Baylor University, Houston, Texas. The drug was given to 12 male patients, aged 29 to 68 years, the dose in most instances being 2·5 mg., although in some it was 5 or 10 mg. A fall of 20 mm. Hg in diastolic pressure in the supine position was noted on the average about 3 hours after the injection, the duration of this response averaging about 10 hours. Side-effects included severe anxiety (2 cases), somnolence, loose stools, and nasal congestion. From this study the authors conclude that intramuscular injection of 2·5 mg. of reserpine at 12-hourly intervals is adequate and possibly the best treatment for hypertensive crises.

K. G. Lowe

931. **Evidence of Decreased Vascular Permeability in Essential Hypertension**
K. KOVACH and B. HEINZEN. *Acta medica Scandinavica* [*Acta med. scand.*] **154**, 111–118, March 26, 1956. 2 figs., 7 refs.

At the Bellevue Hospital, New York, the authors studied the rate at which a single dose of inulin, intravenously administered, disappeared from the plasma of 20 patients with and without hypertension. It was found that the inulin disappeared more slowly from the plasma of patients with severe hypertension than from the plasma of those without signs or symptoms of the disease. This difference is considered to be due to decreased vascular permeability to inulin in the hypertensive subjects. [Although the authors seek to show that the difference could not be due to a lower renal excretion of inulin among the hypertensive patients, a study of their figures leaves the reader in some doubt concerning the true explanation of the difference.]

G. S. Crockett

Correction—The 9 cases of staphylococcal infection following cardiac surgery described in Abstract 371 in the August issue were not all encountered at Sully Hospital, Glamorgan, as stated, but were collected from four different hospitals.

[EDITOR]

Haematology

932. **The Initial Clinical Manifestations of Multiple Myeloma.** (Manifestations cliniques initiales du myélome multiple)

J. LEBON, J. MESSERSCHMITT, and J. AMOUYAL. *Presse médicale* [*Presse méd.*] **64**, 587–588, March 28, 1956. Bibliography.

From an analysis of 116 cases of multiple myeloma, 95 of which were collected from the literature, the remainder not having been previously reported, the authors, working at the Medical Clinic of the University of Algiers, have attempted to determine the earliest clinical manifestations of the disease.

Progressive bone pains, especially in the lumbar region, the sternum, the ribs, or diffusely distributed through the body and often associated with a moderate albuminuria and increased erythrocyte sedimentation rate, are the commonest primary symptoms; occasionally the first manifestations take the form of a non-hypertensive, azotaemic albuminuria, or the patient may present with signs of compression of the spinal cord or a peripheral nerve. These three types of presentation together account for over 75% of cases.

In other cases investigation of a bony or extraosseous tumour, a pathological fracture, haemorrhagic phenomena, severe anaemia, or the picture of a malignant blood dyscrasia leads to the diagnosis of multiple myeloma. In some cases the symptoms and signs are non-specific—for example, pneumopathy, recurrent fever, or a gradual deterioration of the general state—while in cases with systemic amyloidosis the clinical picture is unusual, with predominantly visceral manifestations such as cardiac failure, haemorrhages from the alimentary tract, polyarthritis, muco-cutaneous infiltrations, and even macroglossia.

The authors conclude that the diagnosis of multiple myeloma, which is too frequently the fortuitous result of the finding of suggestive para-clinical signs—radiological, haematological, or biochemical—could be made in many cases from the clinical signs if these were more widely known. *Victor M. Rosenoer*

933. **Treatment of Chronic Granulocytic Leukemia with Myleran**

J. LOUIS, L. R. LIMARZI, and W. R. BEST. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **97**, 299–308, March, 1956. 6 figs., 10 refs.

A study is presented of 32 cases of chronic myeloid leukaemia treated with "myleran" (1:4-bis-(methylsulphonoxy)-butane; busulphan) and observed for not less than one or more than 13 months. In each case the leucocyte count was reduced to normal levels initially, but the need for close haematological supervision is stressed; one patient not so supervised died of marrow aplasia. In 2 cases treated with busulphan subsequent radiotherapy proved to be effective. [This is contrary to the usual experience.] *A. Piney*

934. **Studies on Hemoglobin E. I. The Clinical, Hematologic, and Genetic Characteristics of the Hemoglobin E Syndromes. II. The Incidence of Hemoglobin E in Thailand**

A. I. CHERNOFF, V. MINNICH, S. NA-NAKORN, S. TUCHINDA, C. KASHEMSANT, and R. R. CHERNOFF. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **47**, 455–489 and 490–498, March, 1956. 7 figs., bibliography.

A joint investigation is reported from Washington University School of Medicine, St. Louis, and the Siriraj Hospital, Bangkok, which originated from the observation of a severe form of thalassaemia in 32 individuals in Thailand. In most respects these cases were indistinguishable from those described in numerous reports from the Mediterranean countries and elsewhere. However, the course of the disease was somewhat milder and the proportion of individuals surviving into adult age was unusually large. Furthermore, although one parent usually showed haematological features suggesting thalassaemia minor, the second parent was often quite normal. This was not reconcilable with the thesis that thalassaemia major is a disorder of the homozygote. The possibility was therefore investigated that these cases were due to interaction of a single gene for thalassaemia with a gene for an abnormal haemoglobin since the combination of one gene for thalassaemia with one for haemoglobin S or haemoglobin C gives rise to a syndrome rather like that seen in Thailand. Electrophoretic analysis of the blood of some of the 32 patients led to the discovery of a new form of haemoglobin, haemoglobin E, the chief characteristics of which are described in the present paper.

Haemoglobin E differs from all other haemoglobins on paper electrophoresis at alkaline *p*H, when it moves between haemoglobin C and haemoglobin S. At acid *p*H, however, it moves between haemoglobin A and haemoglobin S. Haemoglobin E was found in association with adult haemoglobin (haemoglobin-E trait) in 36 individuals. Some of them had a variety of minor complaints, but in view of the frequency of incidental disease in Thailand no conclusions could be drawn from this observation, and in view of the fact that at least a proportion were healthy the authors conclude that the haemoglobin-E trait is probably not associated with any disability. The condition originally described must then be regarded as thalassaemia–haemoglobin-E disease. Of the original 32 patients, the condition was severe in 28 and moderately severe in 4. In addition, 6 patients were seen who were believed to be homozygous for haemoglobin E. Their ages ranged from 2 to 40 years and 3 of them were married and had a total of 8 children. All of them were in fair or good health, although a history of tiredness, easy fatiguability, and occasional joint pains could usually be obtained. Examination of the blood showed there to be a mild microcytic normochromic anaemia, with a large number of target cells in

the blood. Resistance of the erythrocytes to hypotonic saline solutions was increased. No sickling occurred in erythrocytes containing haemoglobin E.

In the second part of this paper the results are reported of a study of a sample of the population of Thailand carried out to determine the frequency of haemoglobin-E carriers. Of 1,006 individuals of Thai extraction, 13·6% were found to possess haemoglobin E, whereas it was not found at all among 213 racially unmixed Chinese. The highest incidence of haemoglobin E occurred in Thais from the eastern part of the country, those from the north-eastern region bordering on Laos and Cambodia having an incidence of 32·7%. There appeared to be no negative association between haemoglobin E and malaria in adults. *H. Lehmann*

935. **Applications of the Urinary Tracer Test of Schilling as an Index of Vitamin B_{12} Absorption**
E. H. Reisner, J. P. Gilbert, C. Rosenblum, and M. C. Morgan. *American Journal of Clinical Nutrition* [*Amer. J. clin. Nutr.*] **4**, 134–141, March–April, 1956. 12 refs.

In 27 cases of pernicious anaemia approximately 0·5% of an oral dose of 2 μg. of vitamin B_{12} (cyanocobalamin) labelled with radioactive cobalt was excreted in the urine, as determined by the Schilling test (*J. Lab. clin. Med.*, 1953, **42**, 860, and 1954, **2**, 56; *Abstracts of World Medicine*, 1954, **16**, 42, and 1956, **19**, 50); as much as 4 to 12% was excreted after the ingestion of normal gastric juice, and up to 7% when various preparations of intrinsic factor were given. On the basis of these findings it is suggested that to ensure optimal clinical effects only preparations giving an excretion value of at least 2·5% should be used. Of 13 patients with sprue, 9 had an excretion of 1·1% of the radioactive vitamin ingested; that this was not enhanced by the administration of intrinsic factor was regarded as indicating the presence of a defect in cyanocobalamin absorption not ascribable to intrinsic-factor deficiency. The existence has been demonstrated of a small group of patients with megaloblastic anaemia due to deficient absorption of cyanocobalamin which is not affected by intrinsic-factor preparations and who do not show symptoms of sprue. *F. W. Chattaway*

936. **Pernicious Anemia. I. Remission by Small Oral Doses of Purified Vitamin B_{12}**
S. Estren and L. R. Wasserman. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **91**, 499–503, March, 1956. 3 figs., 10 refs.

The deficiency of intrinsic factor in pernicious anaemia can be overcome by the parenteral administration of vitamin B_{12} (cyanocobalamin), by massive oral administration of vitamin B_{12} (1,000 to 9,000 μg. weekly; 3,000 μg. in a single dose), or by the oral administration of smaller doses of vitamin B_{12} together with intrinsic factor from some outside source.

In 8 cases of pernicious anaemia and one case of non-pernicious megaloblastic anaemia treated at Mount Sinai Hospital, New York, the authors have also obtained remissions with small oral doses of vitamin B_{12} alone, maximal remission resulting in 4 cases and submaximal in 5 from a dosage of 5 to 16·8 μg. daily. The maximum reticulocytosis (up to 22·6%) usually occurred on the 8th or 9th day, after a total dose of 35 to 150 μg. had been given. The remission tended to be shortlived (4 to 6 months) unless followed up by parenteral administration of vitamin B_{12}. In 3 of these 9 cases a subsequent relapse was treated successfully on similar lines, but in 2 others the previous response was not repeated; one of these patients was found to have carcinoma of the stomach and the other responded to parenteral administration of vitamin B_{12}. In one additional case of pernicious anaemia no satisfactory haematological response was obtained to 5 μg. of vitamin B_{12} daily by mouth, but the effect of a higher dosage was not tried.

It is suggested that variations in the response to vitamin B_{12} given by mouth in cases of pernicious anaemia may be explained by variations in the amount of intrinsic factor remaining in the gastric and duodenal mucosa, and that combined treatment with vitamin B_{12} and intrinsic factor should not be undertaken until vitamin B_{12} given alone by mouth has been shown to be ineffective. *Ethel Browning*

937. **Observations on Megaloblastic Anaemias after Primidone**
H. Fuld and E. H. Moorhouse. *British Medical Journal* [*Brit. med. J.*] **1**, 1021–1023, May 5, 1956. 10 refs.

938. **The Treatment of Agranulocytosis with Corticotrophin.** (Применение адренокортикотропного гормона гипофиза при агранулоцитозе)
A. M. Raskin. *Проблемы Эндокринологии и Гормонотерапии* [*Probl. Endokr. Gormonoter.*] **2**, 69–74, No. 1, Jan.–Feb., 1956. 3 figs., 13 refs.

Among its other biological properties, ACTH (corticotrophin) has the power of stimulating the activity of the bone marrow, especially its production of neutrophil granulocytes. Although the successful treatment of agranulocytosis with ACTH and cortisone has been reported by various authors, no report on the subject has hitherto appeared in the Soviet literature. The author now describes the use of ACTH in the treatment of 3 cases of agranulocytosis, 2 of unknown aetiology, and one due to a drug ("neosulphazol"). Two cases of agranulocytosis complicating leucoses were also treated, but in neither was there any effect. Of the first 3 patients, 2 recovered and the third showed a marked rise in the granulocyte count before death occurred from peritonitis. In 2 of these cases severe ulceration of the large intestine occurred, with peritonitis, which was fatal in one and necessitated repeated laparotomy and resulted in a faecal fistula in the other. In this last case the ulceration preceded ACTH treatment and therefore could not be ascribed to it.

The author concludes that in spite of the risk of haemorrhage and perforation the use of ACTH appears to be justified in all cases of agranulocytosis in which other methods of stimulating leucopoiesis have failed. *L. Firman-Edwards*

Respiratory System

939. **The Structure of Lung Parenchyma.** (О структуре паренхимы легкого)
A. G. ÉINGORN. *Архив Патологии* [*Arkh. Patol.*] **18**, 83–91, No. 2, 1956. 7 figs., 19 refs.

The anatomical study of the respiratory elements of the bronchial tree here reported from Moscow was based chiefly on stereoscopic examination of unstained lung tissue. The structural unit of the respiratory part of the lungs is the acinus, which consists of an atrium —the dilated portion of a respiratory bronchiole of the third order—and the alveolar duct leaving this atrium. In the adult there may be between 3 and 17 such alveolar ducts, which divide twice or four times into 2 or 4 branches. In the walls of each alveolar duct the average number of alveoli is 80. In the apices of the lungs the acini are better developed than in the inferior lobes and at the hilum; the measurements of these are given in detail. *L. Crome*

940. **The Use of Enzymes and Wetting Agents in the Treatment of Pulmonary Atelectasis**
S. J. CAMARATA, H. J. JACOBS, and J. E. AFFELDT. *Diseases of the Chest* [*Dis. Chest*] **29**, 388–401, April, 1956. 7 figs.

In the authors' view the most important therapeutic measure in atelectasis is to remove the viscid secretions which block the bronchi. Once the viscosity of these secretions is reduced they can be expectorated, provided there is a good cough reflex. To reduce this viscosity the authors used a wetting agent, " triton A-20 ", which is closely related to " alevaire ", or a proteolytic enzyme, " tryptar ", which will dissolve mucin without injuring living cells. In this paper from the Rancho Los Amigos Respiratory Center for Poliomyelitis, Hondo, California, they report the results obtained in 125 patients with atelectasis. Generally the drugs were given through a nebulizing apparatus, but in some instances the tryptar solution was poured directly into the affected bronchus through a bronchoscope.

In a group of 30 patients without poliomyelitis there was complete clearance of the lung with tryptar in 48 hours. The results obtained in 95 patients convalescent from poliomyelitis are discussed in detail. It is pointed out that atelectasis is a serious complication of this disease because the cough reflex is depressed and in many cases coughing has to be induced artificially. The atelectasis may be acute (under 2 weeks) or chronic. Of 16 patients treated with triton A-20, 9 failed to improve; when, however, these 9 patients were given tryptar there was complete clearance of the lung. Of the 79 patients treated with tryptar only, one failed to respond. Thus, triton A-20 was " less than 50% effective, whereas tryptar was more than 95% successful ". The duration of treatment was directly proportional to the length of time that the atelectasis had been present, but even in cases in which the lobe had been collapsed for 3 months complete resolution was obtained. Toxic signs were negligible, possibly because diphenhydramine (" benadryl ") was administered before treatment.

The authors emphasize certain aspects of this therapeutic approach—namely, that if a good cough is not forthcoming one must be induced, that in patients convalescent from poliomyelitis a tracheotomy is very helpful, and that suitable antibiotics must be used in every case and upper respiratory tract infections controlled. [There is little doubt that this method of treatment will become commoner; as yet, it has been used only on a small scale in Britain.] *Paul B. Woolley*

941. **Management of Carcinoma of the Bronchus**
N. C. OSWALD. *British Medical Journal* [*Brit. med. J.*] **1**, 761–764, April 7, 1956. 15 refs.

The author reviews 272 cases of bronchogenic carcinoma seen by him at the Brompton and St. Bartholomew's Hospitals, London, since 1947. At the time of diagnosis the growth appeared to be confined to the lungs in 51%, had spread to the mediastinum in 23%, and beyond the thorax in 26%, although diagnosis was effected fairly early, the median duration of symptoms from onset to diagnosis being 3½ months. Surgery is undoubtedly the treatment of choice, pneumonectomy offering in the most favourable cases a 5-year survival rate of about 50%; although with radiotherapy the 1-year survival rate may reach this level, the 5-year rate is rarely more than 3%. However, pneumonectomy carries a 10% operative mortality, and when this form of treatment is being considered the general condition of the patient is of paramount importance, since many of the early postoperative deaths are due to medical complications. In the case of radiotherapy, many of its undesirable side-effects can be avoided, providing suitable precautions are taken and that the patient is in fairly reasonable condition. Its greatest value lies in the relief it gives of the distress due to vena caval obstruction, recurrent cough, intractable haemoptysis, and osseous metastases. The author suggests that a dose of 4,000 r spread over 4 to 6 weeks may be as effective as the dose of 6,000 r recently regarded as the minimum.

Of the 272 patients, only 72 were suitable for radical resection or radical radiotherapy. For the rest the prognosis was bad. In this series, of 191 patients followed up for at least a year, 41% were dead within 3 months of diagnosis and 76% within the year. These figures point urgently to the importance of early diagnosis, and also to the necessity for drastically reducing the interval between suspecting the disease and initiating treatment. So far chemotherapeutic agents such as nitrogen mustard have had no beneficial effects. In view of the grave outlook in bronchial carcinoma every conceivable means of improving the prognosis should be diligently pursued, and some of these are briefly considered.
Paul B. Woolley

942. **The Treatment of Metastatic Pulmonary Malignancy**
C. R. KELLY and H. T. LANGSTON. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **31**, 298–315, March, 1956. 6 figs., 8 refs.

In this communication from the University of Illinois College of Medicine the authors review 109 cases (91 from the literature and 18 personal cases) in which pulmonary metastases from a malignant growth were resected; they comprised 65 cases of carcinoma, 38 of sarcoma, and 6 cases in which the nature of the primary growth was not stated. Of 82 of the patients who were followed up for 2 years or more, 19 (8 with carcinoma and 11 with sarcoma) were alive without recurrence, a 2-year survival rate of 23·2%.

It is emphasized that in patients in whom a primary extrapulmonary growth has been controlled, the presence of a discrete pulmonary lesion is an absolute indication for thoracotomy; if it is a metastasis there is a fair chance of controlling it, but there is also a real possibility that the lesion may be a second primary growth. The authors' criteria for exploration are: (1) that the primary growth has been completely eradicated; (2) that there is no evidence of other metastases elsewhere; and (3) that the pulmonary lesion is a single, discrete tumour, preferably confined to one lobe or segment. Particulars of their own 18 cases are tabulated, 6 of them being described in detail and illustrated with radiographs and photomicrographs. The majority were treated by localized (segmental or wedge) resection. They conclude that surgical excision of metastatic malignant growths of the lung is technically feasible " and productive of a significant group of long-term survivors in selected cases ". *F. J. Sambrook Gowar*

943. **Lobectomy for Bronchial Carcinoma**
J. R. BELCHER. *Lancet* [*Lancet*] **1**, 349–353, April 7, 1956. 8 figs., 17 refs.

In view of the lower mortality and the smaller reduction in pulmonary function associated with lobectomy as compared with pneumonectomy, the author, in this paper from the Middlesex Hospital, London, attempts to assess the value of lobectomy as the operation of choice in bronchial carcinoma. The conclusions reached are based on 264 cases operated on by a number of surgeons (49 by the author) between 1949 and 1953.

Of the 264 patients, 12 (4%) died at or soon after operation, and of the remainder, 145 (57%) survived a year or more; of 96 operated on over 2 years previously 45 were alive, of 46 operated on over 4 years previously 25 were alive, while of 18 subjected to operation 5 or more years before 11 were alive. The prognosis was slightly poorer in cases of " circumscribed " tumours (as defined by Rabin and Neuhof) than in cases of " uncircumscribed " lesions. The survival rate was highest among patients with adenocarcinomata, but the 2-year survival rate of patients with undifferentiated tumours was similar to that of patients with squamous-celled tumours (43% and 46% respectively). The 2-year survival rate was considerably lower in the group of cases with lymph-node involvement (35%) than in those in which there was no such involvement (54%). The site of the tumour did not appear to influence the prognosis. As expected, the prognosis was better when resection was performed as a policy than when it was undertaken as a palliative measure. Even so, of patients in whom the extent of the tumour warranted pneumonectomy but in whom lobectomy was performed because of age or poor respiratory reserve, 33% survived over 2 years.

The cause was known in 113 of the 119 deaths in the series; of 101 late deaths, 19 were due to causes other than carcinoma, 55 to general metastases, and 27 to local involvement. As regards the last group it is thought possible that some of these 27 patients might have survived if a more radical procedure had been carried out; on the other hand, the proportion who died from local metastases was small and corresponded closely with that reported by Aylwin in a series of patients subjected to pneumonectomy. While it may be argued that the patients in the present series were selected when the tumour was localized, before lymph-nodes were involved, and favourable results could therefore be expected, the author notes that according to Bignall and Moon comparison of the results of lobectomy and pneumonectomy on the basis of the presence or absence of lymph-node metastases fails to reveal any difference in favour of the more extensive operation.

The survival rate in this series compares favourably with that observed by others after pneumonectomy. This and the fact that lobectomy is a less crippling procedure justify, in the author's view, a " continuation of the policy of lobectomy where possible in the treatment of bronchial carcinoma ". [The evolution of a truly " radical lobectomy " based on an accurate knowledge of the lobar lymphatic drainage would establish this procedure more firmly.] *A. M. Macarthur*

944. **Clinical Studies in the Aetiology of Bronchial Carcinoma.** (Klinische Studien zur Aetiologie des Bronchialkarzinoms)
O. GSELL. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **81**, 496–501, April 6, 1956. 1 fig., 37 refs.

In this contribution to the aetiology of bronchial carcinoma from the University Policlinic, Basle, the author's findings are based on a study of 165 cases of bronchial carcinoma in males and 15 in females, and on a detailed inquiry into the smoking habits of 150 of the male patients and of 150 male subjects of the same age who were suffering from conditions other than carcinoma. Neither endogenous factors referable to heredity, concurrent pulmonary or extrapulmonary disease, nor exogenous factors, such as asbestosis or social status, were found to be aetiologically significant. The study of tobacco consumption, however, was more rewarding. Patients were divided into categories of non-smokers, light smokers (1 to 9 cigarettes daily), moderate smokers (10 to 14 daily), heavy smokers (15 to 20 daily), and very heavy smokers (over 21 cigarettes daily). Among the patients with bronchial carcinoma only 1·3% were non-smokers, while 85% smoked over 15 cigarettes daily; of the control group 19% were non-smokers, and only 32% smoked over 15 cigarettes daily. The author found

that the amount of tobacco smoked, and possibly also the amount inhaled, bore a direct relation to the incidence of bronchial carcinoma in each decade from 40 to 80 years. He believes that smoking is an aetiological factor only in the anaplastic and not in the adenocarcinomatous type of bronchogenic carcinoma. In the group of very heavy smokers carcinoma of the anaplastic type was met with twice as often as the adenocarcinomatous type, while in the whole series 90% of cases of bronchial carcinoma in males were of the anaplastic type and over 50% of the adenocarcinomatous type occurred in women.

The author states that tobacco consumption in Switzerland increased tenfold between 1924, when statistics first became available, and 1952. He estimates that in a country in which one-fifth of the men and four-fifths of the women are non-smokers the tobacco consumption in 1952 for every adult over 15 years of age works out at 4 cigarettes daily. The death rate from bronchogenic carcinoma in Switzerland between 1899 and 1952 has risen 44-fold in men but only 9-fold in women. In 1952 bronchogenic carcinoma was the cause of 14% of all deaths from carcinoma in males, and of 2·2% in females; it was the commonest type of carcinoma in men aged 45 to 54, the second commonest in men aged 55 to 74, the third commonest in men aged 75 to 79, and the seventh in men of 85 and over. In women bronchial carcinoma ranked ninth at all ages from 45 to 70 years.

The author believes that 3:4-benzpyrene is the main carcinogenic substance in tobacco. He estimates that a man smoking 40 cigarettes daily absorbs 150 μg. of benzpyrene yearly in droplet form, and therefore absorbable, and that 98% is retained in the lungs. In addition, the heavy smoker inhales, in common with all city dwellers, air polluted by 200 μg. of 3:4-benzpyrene yearly; the latter, however, is adsorbed on coal particles, which renders it less harmful. He concludes by pointing out that since a constitutional disposition to carcinoma, increasing age, and factors other than smoking, which, may all play some part in the aetiology of bronchial carcinoma, cannot be influenced in any way, the most rapid prophylactic measure at present possible is an immediate reduction in the quantity of tobacco smoked, together with the improvement of cigarette filters, and possibly the elaboration of methods of eliminating carcinogenic substances from tobacco. *E. S. Wyder*

945. **The Pleural Form of Primary Cancer of the Lung**
G. Babolini and A. Blasi. *Diseases of the Chest* [*Dis. Chest*] **29**, 314–323, March, 1956. 8 figs., 9 refs.

In this paper from the University Phthisiological Clinic and the Istituto "Principi di Piemonte", Naples, the authors describe a form of primary carcinoma of the lung which is mainly confined to the pleural surface. They found 5 such cases among 82 patients with primary lung cancer, in 4 of which the diagnosis was confirmed post mortem and in one by thoracoscopy and biopsy. The patients' ages ranged from 43 to 68 years, and the total duration of the illness from 6 to 11 months. All complained of persistent thoracic pain refractory to analgesics, while dyspnoea also was marked, even in the early stages. There was hardly any cough or sputum, and no haemoptysis. At necropsy the neoplastic tissue was almost entirely spread upon the pleural surface of the lung giving an appearance similar to that of primary cancer of the pleura, from which, however, it could be differentiated by histological examination, which revealed the presence of cells of broncho-alveolar origin, often in an abundant collagenous stroma, of various types including small undifferentiated cells, cylindrical cells, and adenocarcinomatous, mucigenous structures. Hilar or pulmonary involvement was not marked, and there was no extensive intrabronchial proliferation. In most cases there was an accompanying large serofibrinous or haemorrhagic pleural effusion which readily reformed after aspiration. In some cases metastases were found in the regional lymph nodes, liver, kidneys, and adrenal glands.

The authors suggest that this type of neoplasm may start either in the subpleural lung parenchyma or in the bronchoalveolar segment adjacent to the mediastinal pleura, with progressive involvement of the pleural lymphatic system in the former case and retrograde involvement in the latter. *I. Ansell*

946. **Pulmonary Emphysema Treated with Pneumoperitoneum**
O. Neufeld. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] **4**, 328–335, April, 1956. 8 figs.

This paper reports the results obtained with therapeutic pneumoperitoneum in 14 patients aged 46 to 63 with far-advanced pulmonary emphysema due to chronic bronchial infection but with no definite evidence of heart failure. The author considered that there was subjective and objective improvement in all except one instance. He suggests that pneumoperitoneum is a valuable procedure in the management of pulmonary emphysema and should be used more frequently in early cases, in which he considers that the pathological process may be reversible. [His conclusions, however, appear to be based on clinical observations alone and are not supported by the results of pulmonary function tests.]
J. N. Harris-Jones

947. **A Theory of the Origin of Intralobar Sequestration of Lung**
R. A. Smith. *Thorax* [*Thorax*] **11**, 10–24, March, 1956. 11 figs., 42 refs.

In the condition of intralobar sequestration of the lung, a large, elastic-walled, aberrant artery arising from the aorta supplies an abnormal bronchopulmonary mass in the posterior portion of the lower lobe. The sequestrated segment has no blood supply from the pulmonary artery, although its venous drainage is to the pulmonary vein. The condition is slightly more common on the left side (in the ratio of about 3:2), and it is not associated with other congenital anomalies. The pulmonary changes in the affected segments include alveolar fibrosis, emphysema, mucoid-containing cysts, and in some cases extensive cystic bronchiectasis. The condition can be clearly differentiated from accessory

lung ("extralobar sequestration") on the following grounds: in the latter the systemic arterial supply is small and may arise from intercostal or phrenic arteries as well as from the aorta, the venous drainage is to the azygos system, associated congenital abnormalities (such as diaphragmatic hernia) are frequent, and in almost all cases (90%) the condition is left-sided.

In this paper from the King Edward VII Memorial Chest Hospital, Warwick, the author discusses various theories of the aetiology of intralobar sequestration and reports 2 further cases of the condition in males aged 18 and 25 respectively. He suggests that the primary abnormality is failure of the peripheral branches of the primitive pulmonary artery to develop. As a consequence, a systemic supply from the aorta persists and the high intravascular pressure present after birth causes progressive cystic degeneration and fibrosis of the lung. The affected segment may subsequently become infected and give rise to the usual clinical picture of bronchiectasis.

E. Keith Westlake

948. **Bronchiectasis as a Surgical Disease. Long-term Results of Operation in 145 Cases. A Clinical and Bronchographic Study.** (La bronchectasie est-elle une maladie chirurgicale? Résultats éloignés chez 145 operés. Étude clinique et bronchographique)
J. MATHEY, J. J. GALEY, G. OUSTRIÈRES, and G. VERMEIL. *Semaine des hôpitaux de Paris* [*Sem Hôp. Paris*] **32**, 1186–1194, April 6, 1956. 9 refs..

The authors assess the place of surgery in the treatment of bronchiectasis with reference to their own series of 145 patients on whom 152 resections were carried out. There were 4 operative deaths in this series, 2 of which occurred among the first 10 cases at a time when tourniquet resection was still practised. There were 7 late deaths, 2 from pulmonary tuberculosis, 3 from causes related to residual bronchiectasis, and 2 from unrelated causes. Of the 133 survivors, 91 are regarded as cured and 24 as improved, with 18 failures. Among the 82 cases of unilateral disease the failures were due to bronchiectasis appearing in the remaining lung, as shown on several occasions by postoperative bronchography. Cases of bilateral disease can be divided into those with asymmetrical involvement, which are usually much improved by resection confined to the more severely affected side, and those of symmetrical disease, in which bilateral operation is necessary.

A study of those cases in which the postoperative course is unsatisfactory shows that residual bronchiectasis on the operated side almost always gives rise to symptoms, whereas contralateral residual disease may cause none. Bronchiectasis may appear after operation in a segment which was previously normal, or pre-existing bronchiectasis may become more severe. The authors do not consider the normal lingula to be particularly liable to develop bronchiectasis postoperatively, but the conservation of dorsal segments after resection of the basal segments of the lower lobe may often lead to bronchiectasis in that segment. This type of bronchiectasis need not be permanent, however, and in their opinion it is worth while to preserve the dorsal segment of the lower lobe. Cases in which bronchiectasis develops in one lobe as a consequence of local bronchial obstruction do better than those in which the disease is associated with bronchitis and multiple lesions. In the latter type of case operation should be carried out only after a prolonged period of medical treatment, when the residual lesions appear to be irreversible.

Though the operative risks of resection in bronchiectasis are small, good results can be obtained only by the careful selection of cases, bearing in mind the importance of perfect preoperative bronchography, by limiting resection to areas of localized, gross disease and by careful postoperative management with a view to the avoidance of atelectasis and bronchopleural fistula, complications which favour the development of fresh areas of bronchiectasis.

A. M. Macarthur

949. **The Effect of Hydrocortisone upon the Course of Pneumococcal Pneumonia Treated with Penicillin**
H. N. WAGNER, I. L. BENNETT, L. LASAGNA, L. E. CLUFF, M. B. ROSENTHAL, and G. S. MIRICK. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **98**, 197–215, March, 1956. 8 figs., 39 refs.

Although it is known that the course of an infection which develops in patients already receiving cortisone is often rapidly progressive, the authors, at Johns Hopkins Hospital, Baltimore, decided to study the effect of hydrocortisone on the course of pneumococcal pneumonia treated with penicillin, an illness which runs a rather predictable course. Of 113 patients with pneumococcal pneumonia admitted to the hospital during an 8-month period, 52 received a 5-day course of hydrocortisone by mouth in addition to penicillin and 61, the control group, received penicillin only. The two groups were comparable as regards age and sex of the patients and prognosis. One death occurred in each group, from causes other than the pneumonia.

No suppurative complications were observed in either group, and a sterile pleural effusion was present in the same number of cases in each. The length of time taken for complete resolution was the same in the two groups. None of the common side-reactions of steroid therapy occurred. The only disturbing toxic reaction attributable to the hydrocortisone was severe hypothermia in one patient, necessitating withdrawal of the drug. (One patient who did not receive hydrocortisone had a massive haematemesis.) There was more rapid symptomatic improvement in the patients receiving hydrocortisone than in those given penicillin only. Thus the temperature fell to normal more quickly in the cortisone-treated group, although in some cases the rebound phenomenon occurred. Appetite became normal in an average of 3 days compared with 4 days in the controls. Pain decreased within 24 hours in all the 24 cases in the hydrocortisone group specially studied, but in only 18 out of 21 in the control group, while the average time for complete relief of pain was 2 days in the treated and 4 in the control group.

The authors conclude that their results justify further cautious use of corticosteroids as adjuvants to specific antibacterial therapy.

A. Gordon Beckett

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R. A. Smith. *Thorax* [*Thorax*] **11**, 10–24, March, 1956. 11 figs., 42 refs.

In the condition of intralobar sequestration of the lung, a large, elastic-walled, aberrant artery arising from the aorta supplies an abnormal bronchopulmonary mass in the posterior portion of the lower lobe. The sequestrated segment has no blood supply from the pulmonary artery, although its venous drainage is to the pulmonary vein. The condition is slightly more common on the left side (in the ratio of about 3:2), and it is not associated with other congenital anomalies. The pulmonary changes in the affected segments include alveolar fibrosis, emphysema, mucoid-containing cysts, and in some cases extensive cystic bronchiectasis. The condition can be clearly differentiated from accessory

lung ("extralobar sequestration") on the following grounds: in the latter the systemic arterial supply is small and may arise from intercostal or phrenic arteries as well as from the aorta, the venous drainage is to the azygos system, associated congenital abnormalities (such as diaphragmatic hernia) are frequent, and in almost all cases (90%) the condition is left-sided.

In this paper from the King Edward VII Memorial Chest Hospital, Warwick, the author discusses various theories of the aetiology of intralobar sequestration and reports 2 further cases of the condition in males aged 18 and 25 respectively. He suggests that the primary abnormality is failure of the peripheral branches of the primitive pulmonary artery to develop. As a consequence, a systemic supply from the aorta persists and the high intravascular pressure present after birth causes progressive cystic degeneration and fibrosis of the lung. The affected segment may subsequently become infected and give rise to the usual clinical picture of bronchiectasis.

E. Keith Westlake

948. **Bronchiectasis as a Surgical Disease. Long-term Results of Operation in 145 Cases. A Clinical and Bronchographic Study.** (La bronchectasie est-elle une maladie chirurgicale? Résultats éloignés chez 145 opérés. Étude clinique et bronchographique)
J. MATHEY, J. J. GALEY, G. OUSTRIÈRES, and G. VERMEIL. *Semaine des hôpitaux de Paris* [*Sem Hôp. Paris*] **32**, 1186–1194, April 6, 1956. 9 refs..

The authors assess the place of surgery in the treatment of bronchiectasis with reference to their own series of 145 patients on whom 152 resections were carried out. There were 4 operative deaths in this series, 2 of which occurred among the first 10 cases at a time when tourniquet resection was still practised. There were 7 late deaths, 2 from pulmonary tuberculosis, 3 from causes related to residual bronchiectasis, and 2 from unrelated causes. Of the 133 survivors, 91 are regarded as cured and 24 as improved, with 18 failures. Among the 82 cases of unilateral disease the failures were due to bronchiectasis appearing in the remaining lung, as shown on several occasions by postoperative bronchography. Cases of bilateral disease can be divided into those with asymmetrical involvement, which are usually much improved by resection confined to the more severely affected side, and those of symmetrical disease, in which bilateral operation is necessary.

A study of those cases in which the postoperative course is unsatisfactory shows that residual bronchiectasis on the operated side almost always gives rise to symptoms, whereas contralateral residual disease may cause none. Bronchiectasis may appear after operation in a segment which was previously normal, or pre-existing bronchiectasis may become more severe. The authors do not consider the normal lingula to be particularly liable to develop bronchiectasis postoperatively, but the conservation of dorsal segments after resection of the basal segments of the lower lobe may often lead to bronchiectasis in that segment. This type of bronchiectasis need not be permanent, however, and in their opinion it is worth while to preserve the dorsal segment of the lower lobe. Cases in which bronchiectasis develops in one lobe as a consequence of local bronchial obstruction do better than those in which the disease is associated with bronchitis and multiple lesions. In the latter type of case operation should be carried out only after a prolonged period of medical treatment, when the residual lesions appear to be irreversible.

Though the operative risks of resection in bronchiectasis are small, good results can be obtained only by the careful selection of cases, bearing in mind the importance of perfect preoperative bronchography, by limiting resection to areas of localized, gross disease and by careful postoperative management with a view to the avoidance of atelectasis and bronchopleural fistula, complications which favour the development of fresh areas of bronchiectasis.

A. M. Macarthur

949. **The Effect of Hydrocortisone upon the Course of Pneumococcal Pneumonia Treated with Penicillin**
H. N. WAGNER, I. L. BENNETT, L. LASAGNA, L. E. CLUFF, M. B. ROSENTHAL, and G. S. MIRICK. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **98**, 197–215, March, 1956. 8 figs., 39 refs.

Although it is known that the course of an infection which develops in patients already receiving cortisone is often rapidly progressive, the authors, at Johns Hopkins Hospital, Baltimore, decided to study the effect of hydrocortisone on the course of pneumococcal pneumonia treated with penicillin, an illness which runs a rather predictable course. Of 113 patients with pneumococcal pneumonia admitted to the hospital during an 8-month period, 52 received a 5-day course of hydrocortisone by mouth in addition to penicillin and 61, the control group, received penicillin only. The two groups were comparable as regards age and sex of the patients and prognosis. One death occurred in each group, from causes other than the pneumonia.

No suppurative complications were observed in either group, and a sterile pleural effusion was present in the same number of cases in each. The length of time taken for complete resolution was the same in the two groups. None of the common side-reactions of steroid therapy occurred. The only disturbing toxic reaction attributable to the hydrocortisone was severe hypothermia in one patient, necessitating withdrawal of the drug. (One patient who did not receive hydrocortisone had a massive haematemesis.) There was more rapid symptomatic improvement in the patients receiving hydrocortisone than in those given penicillin only. Thus the temperature fell to normal more quickly in the cortisone-treated group, although in some cases the rebound phenomenon occurred. Appetite became normal in an average of 3 days compared with 4 days in the controls. Pain decreased within 24 hours in all the 24 cases in the hydrocortisone group specially studied, but in only 18 out of 21 in the control group, while the average time for complete relief of pain was 2 days in the treated and 4 in the control group.

The authors conclude that their results justify further cautious use of corticosteroids as adjuvants to specific antibacterial therapy.

A. Gordon Beckett

Otorhinolaryngology

950. **Closure and Opening of the Larynx during Swallowing**

G. M. ARDRAN and F. H. KEMP. *British Journal of Radiology* [*Brit. J. Radiol.*] **29**, 205–208, April, 1956. 2 figs., 6 refs.

A series of cineradiographic studies of the laryngeal region in the antero-posterior projection during the swallowing of barium emulsion was undertaken at Norrtull's Hospital, Stockholm, on 5 boys aged 15 to 17 years. They showed that closure of the larynx is from below upwards, the contents of the laryngeal vestibule being expressed into the pharynx, and that opening also is from below upwards.

The movement of the various parts is described in detail. Closure of the larynx is accomplished essentially by sphincteric action of the upper part of the larynx, but also in part by a valvular mechanism with approximation (limiting inspiration) of the vocal folds. Studies of the radiographic appearances of the laryngeal ventricle show that its cavity is directed laterally and outwards, or laterally and downwards, but never laterally and upwards as previously described. This is one of the factors which lead the authors to reject the theory of Negus that the vestibular folds perform a valvular function, limiting expiration.

[The features described may well be visible in the original films, but the abstracter is unable to determine their presence in the reproductions of single frames which accompany the article.] *T. A. Clarke*

951. **The Problem of Otitis Externa**

C. KEOGH and B. RUSSELL. *British Medical Journal* [*Brit. med. J.*] **1**, 1068–1072, May 12, 1956. 3 figs., 21 refs.

A clinical and bacteriological examination was carried out on 100 out-patients attending the otological and dermatological departments (50 patients each) of the London Hospital. In the former group the disease tended to be confined to the auditory canal, whereas in the latter, the concha and auricle were often also involved. *Staphylococcus pyogenes* accounted for the infection in 75 cases. The bacteriological findings could be classified in three main groups: pathogenic cocci, intestinal pathogens, and saprophytes (the figures and percentages of these are tabulated). In 56 patients, the ears were contaminated with intestinal organisms. Infection may arise from organisms already in the ear, or it may be transferred on the fingers from the nose, from boils, ulcers, or areas of infective dermatitis. Faecal contamination, especially in patients with pruritus and a low standard of hygiene, plays a prominent part.

The clinical appearances are described, and a list of 17 skin diseases which may accompany otitis externa is given. Trauma (in the form of scratching, fingering, or the abuse of wax solvents), emotional disturbances, climatic conditions, and allergy are all possible factors in causation. Prevention depends on the avoidance of any form of trauma to the meatal skin, and in personal cleanliness. Treatment consists in meticulous cleaning of the meatus, elimination of the infective state, restoring the protective mechanism of the meatal skin, and relieving any aural pruritus. The use of the various antibiotics is discussed. Sulphonamides, penicillin, and streptomycin tend to sensitize the skin, and should not be used.

H. D. Brown Kelly

952. **Results of Treatment of Otitic and Sinus Barotrauma**

E. D. D. DICKSON and P. F. KING. *Journal of Aviation Medicine* [*J. Aviat. Med.*] **27**, 92–99, April, 1956. 9 refs.

The authors discuss a series of 350 cases of otitic or sinus barotrauma in 328 patients (22 having both conditions) observed at the Central Medical Establishment of the R.A.F., London, during a 3-year period. These patients were referred by their unit medical officer because they presented some difficulty in their management or disposal.

Of 250 cases of otitic barotrauma, all first received simple treatment (nasal decongestion, inflation of the middle ear, aspiration of fluid from the middle ear, or long-term treatment for chronic or allergic rhinitis). In 162 cases no further treatment was necessary; in 41 cases surgery was undertaken, mainly to improve the aeration of the nose or sinuses, 80% of these patients being able to return to full flying duty; and 25 patients who failed to respond to simple and surgical treatment were given deep *x*-ray therapy to one or both eustachian tubes, 8 being returned to full flying duties.

Of 100 cases of sinus barotrauma, one or both of the frontal sinuses were involved in 80, the antrum was involved in 29, and the ethmoid cells in one. All received simple treatment—nasal decongestion, antral lavage, or long-term treatment for chronic or allergic rhinitis—while in a few cases antihistaminics were used during an acute phase, but the danger of side-effects while flying prevented their use over a long period. Such treatment was sufficient in 38 cases, in 25 (66%) of which the patient returned to full flying duties. In 40 cases surgery was undertaken, mainly to improve the aeration and drainage of the nose and sinuses; 31 (77%) of these patients were returned to full flying duties.

Of the whole series, 70% were returned to full flying duties, 13% to restricted flying, and 17% were grounded (except as passengers), there being no marked difference in the results of treatment between the cases of otitic and sinus barotrauma. In 18 cases of otitic barotrauma the patient had a ruptured tympanic membrane, but this had no apparent effect on the ultimate disposal of these patients compared with others with otitic barotrauma.

Norman W. MacKeith

Urogenital System

953. **Renal Tubular Acidosis**
G. L. Foss, C. B. Perry, and F. J. Y. Wood. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **25**, 185–199, April, 1956. 3 figs., 32 refs.

After a short review of previous descriptions of the rare clinical syndrome of renal tubular acidosis, in which there is a failure of the kidneys to produce urine of normal acidity, the authors describe 5 further cases seen at Bristol Royal Hospital and the Royal South Hants Hospital, Southampton. The patients included a brother and sister, and reasons are given for the belief that the condition may be familial, even in those patients who develop symptoms only in adult life. The mechanism of the failure of acidification of the urine is discussed, and also the possibility that loss of potassium leads to further renal damage. In a long discussion the authors comment on treatment and prognosis; the danger of giving sulphonamides or other inhibitors of carbonic anhydrase to these patients, for example, in the treatment of a urinary infection, is once again stressed, the authors describing a personal experience of the deleterious action of sulphonamide in this condition.

D. A. K. Black

954. **Salt Loss in Chronic Renal Disease**
A. E. Read. *British Medical Journal* [*Brit. med. J.*] 1, 1399–1401, June 16, 1956. 14 refs.

955. **The Use of Heparin in the Treatment of Lipoid Nephrosis.** (Utilité de l'héparine dans le traitement de la néphrose lipoïdique)
Y. Boquien and J. F. Porge. *Presse médicale* [*Presse méd.*] **64**, 692, April 14, 1956.

The authors have successfully treated 6 cases of "lipoid nephrosis" with heparin, a diuresis and resolution of the oedema being obtained in each case. Three of these cases are reported in some detail. A girl of 3½ years, who had developed the nephrotic syndrome following a sore throat, still had oliguria, albuminuria, scanty granular casts and blood in the urine and a raised blood urea content after 5 months. The daily intramuscular injection of 80 mg. of heparin produced an immediate diuresis, but on two occasions when treatment was stopped the oedema recurred. With the institution of "maintenance treatment" with 40 mg. heparin intramuscularly 2 to 4 times a month the oedema is now almost absent, but the biochemical changes of lipoid nephrosis persist. The second case was that of a hypertensive man of 56 who developed oedema following treatment with a mercurial compound. There was marked albuminuria, erythrocytes and granular casts in the urine, slight azotaemia, and a raised plasma cholesterol level. Heparin therapy was followed by complete resolution of the oedema, and at follow-up more than a year later there was no evidence of nephrotic changes clinically or in the blood or urine. The third patient, a man of 38, developed renal insufficiency after lipoid nephrosis of 9 years' duration. Heparin reduced the degree of albuminuria and caused disappearance of the oedema, but did not affect the azotaemia.

The dosage of heparin was empirical. The authors suggest that for the first 10 or 12 days 100 mg. may be given daily, intravenously if possible, in 2 doses, further treatment being continued with the intramuscular "retard" preparation; the initial doses for children were 50 to 80 mg. There were no troublesome side-effects. The authors point out that heparin merely reduces the oedema and does not produce a cure of the renal condition.

T. B. Begg

956. **Nitrofurantoin (Furadantin) in Treatment of Urinary Tract Infections**
B. L. Stewart and H. J. Rowe. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 1221–1223, April 7, 1956.

Nitrofurantoin ("furadantin") was tried in the treatment of acute and chronic urinary infections in a total of 112 patients of all ages from 3 years upwards. In 73 chronic cases there was persistent or recurrent infection in spite of treatment with sulphonamides and antibiotics, and in many pronounced structural defects were present.

Nitrofurantoin was given by mouth in a dosage of 100 mg. 3 or 4 times daily (50 mg. 2 or 3 times a day in children) and was continued for 2 weeks if necessary. In 81% of the cases there was symptomatic and bacteriologic "cure" for at least 6 weeks after treatment ended, but the final cure rate was 57%. Of the 27 recurrences only one was in an acute case. Symptoms were alleviated in 24 to 36 hours, and cultures were sterile in 8 to 36 hours. Nitrofurantoin was extremely effective against most organisms, but not *Staphylococcus aureus*, *Proteus vulgaris*, or *Proteus mirabilis*. *Staphylococcus aureus* continued to grow, or reappeared, in 67% of the cases in which it was isolated, the figures for *P. vulgaris* and *P. mirabilis* being, respectively, 83% and 100%. The organisms most frequently isolated were *Escherichia coli* and *Aerobacter aerogenes*. In 2 cases of infection due to *Pseudomonas* sp. a cure was obtained, which was unexpected, but both cases were acute and uncomplicated. Side-effects, which occurred in 13 cases, included nausea, vomiting, chills, fever, rash, dizziness, dermatitis medicamentosa, and biliuria. Nausea was not observed when the drug was given with meals.

T. B. Begg

957. **Treatment of Urinary Tract Infection with Triple Sulfonamides and a Penicillin–Triple Sulfonamide Mixture. A Comparative Study**
A. W. Bohne and W. E. Chase. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **231**, 389–393, April, 1956. 23 refs.

Endocrinology

958. **The Relation between Extracellular and Intracellular Water in Acromegaly.** [In English]
D. IKKOS, H. LJUNGGREN, and R. LUFT. *Acta endocrinologica* [*Acta endocr.* (*Kbh.*)] **21**, 211–225, March, 1956. 10 figs., 14 refs.

The results of the determination of extracellular water with thiosulphate as the parameter have been shown to be not always reliable. The authors have therefore re-examined this problem and, in a study carried out at the Serafimer Hospital, Stockholm, have determined the relation between the extracellular and intracellular water and also the amount of exchangeable potassium in 24 patients with acromegaly, but no evidence of cardiac insufficiency, and 47 normal subjects. Extracellular water was determined by the volumes of distribution of inulin, exchangeable sodium, and exchangeable chloride; intracellular water was determined by direct measurement or from the apparent volume of distribution of thiosulphate, and cell mass by measurement of the exchangeable potassium. It was found that extracellular water was increased in relation to intracellular water and to cell mass in the patients with acromegaly. The different parameters used in determining the extracellular water showed no significant differences between the acromegalic patients and the normal subjects. *F. W. Chattaway*

959. **Glomerular Filtration Rate and Renal Plasma Flow in Acromegaly.** [In English]
D. IKKOS, H. LJUNGGREN, and R. LUFT. *Acta endocrinologica* [*Acta endocr.* (*Kbh.*)] **21**, 226–236, March, 1956. 3 figs., 15 refs.

Because of the intimate relationship between renal function and the distribution of body water the authors compared the glomerular filtration rate, renal plasma flow, and body water compartments in 13 patients with acromegaly (see Abstract 958), and in 22 healthy subjects. The glomerular filtration rate was found to be increased in the acromegalic patients relative to body surface area, total body water, and intracellular water; the renal plasma flow was also higher in this group in relation to the intracellular water and probably also in relation to total body surface. However, in relation to extracellular water the values for glomerular filtration rate and renal plasma flow showed no significant differences in the two groups. It is concluded that in acromegaly these values show parallel changes. The detailed results are tabulated. *F. W. Chattaway*

960. **Basal Metabolic Rate in Relation to Body Size and Cell Mass in Acromegaly.** [In English]
D. IKKOS, H. LJUNGGREN, and R. LUFT. *Acta endocrinologica* [*Acta endocr.* (*Kbh.*)] **21**, 237–244, March, 1956. 1 fig., 10 refs.

The calculation of the basal metabolic rate (B.M.R.) in relation to weight and height may give erroneous results in patients with acromegaly, since the height of these patients is frequently apparently reduced by the presence of kyphosis and kyphoscoliosis. At the Serafimer Hospital, Stockholm, the authors have therefore determined the B.M.R. in 15 patients with acromegaly and in 31 normal subjects, using the cell mass as the standard of reference. The B.M.R. was shown to be consistently higher in the acromegalic patients than in the control subjects, and this increase was the same whether the B.M.R. was determined on the basis of body size or cell mass. It is concluded that this finding probably justifies the continued use of body size as a basis for calculating the B.M.R. *F. W. Chattaway*

THYROID GLAND

961. **Treatment with Small Doses of Thyroidin of Patients with Hypothyroidism Complicated by Coronary Atherosclerosis.** (Лечение малыми дозами тиреоидина больных гипотиреозом осложненным коронарным атеросклерозом)
V. G. BARANOV and V. M. DIL'MAN. *Проблемы Эндокринологии и Гормонотерапии* [*Probl. Endokr. Gormonoter.*] **2**, 13–19, No. 1, Jan.–Feb., 1956. 6 figs., 7 refs.

Experimental work has demonstrated the importance of hypercholesterolaemia in the pathogenesis of atherosclerosis, which can in fact be regarded as a disturbance of cholesterol metabolism. The thyroid gland is a regulator of this metabolism, and a rise in the blood cholesterol level is one of the earliest signs of hypothyroidism. Intact dogs may be fed on a high-cholesterol diet without the development of hypercholesterolaemia, but after surgical ablation of the thyroid or administration of methylthiouracil both hypercholesterolaemia and atherosclerosis are produced. On the other hand the development of atherosclerosis in rabbits given a high-cholesterol diet can be prevented by giving thyroidin, with reversion of early arterial changes to normal.

Patients with hypothyroidism, hypercholesterolaemia, and atherosclerosis often complain of symptoms of coronary insufficiency on exertion. The present authors claim that it is possible in these cases to reduce the blood cholesterol content by means of thyroidin in small doses (0·15 g. 2 or 3 times daily) without increasing the basal metabolic rate (B.M.R.) and so precipitating an anginal attack.

A case is described in which the blood cholesterol level fell from 400 mg. to 280 mg. per 100 ml. with such treatment, the B.M.R. remaining constant at −36%. After 31 days of treatment there was a marked improvement in the frequency and severity of the anginal attacks. Over 2 years' observation the blood cholesterol level fluctuated between 170 and 300 mg. per 100 ml.,

and the patient's general condition remained satisfactory. In spite of the subnormal B.M.R., his capacity for work was but little impaired.

The authors state that the use of thyroidin in small doses is also valuable in those cases of angina and cardiac failure which have been treated by thyroidectomy or with thiouracil or radioactive iodine.

L. Firman-Edwards

962. **Psychophysiology and Psychiatric Management of Thyrotoxicosis: a Two Year Follow-up Study**
H. J. KLEINSCHMIDT, S. E. WAXENBERG, and R. CUKER. *Journal of the Mount Sinai Hospital* [*J. Mt Sinai Hosp.*] 23, 131–153, March–April, 1956. 23 refs.

At the Mount Sinai Hospital, New York, 84 patients with thyrotoxicosis were subjected to psychiatric examination, each patient being interviewed at least twice and many of them on a number of occasions subsequently. The history in 81 of the 84 cases contained clear evidence of an emotional precipitation of the illness. Altogether 30 patients (26 females) were followed up for a period of 2 years, 27 being given a battery of psychological tests. The classification of these 30 cases was as follows: schizophrenia 4, character disorder 8, manifestations of anxiety, obsessive-compulsive mechanisms, and depression, 13, and borderline cases 5.

The events which were considered to have precipitated the illness were within the range of usual life experience, and were important only because they touched upon particular conflicts in the patient. No specific personality type was observed, and there were no common features in the precipitating experiences or the patterns of conflict. Disturbance of affect, manifested in excessive anxiety, destructive aggression, and depression, was an outstanding feature. The factor of inheritance was thought to be significant.

In the authors' view a probing or searching approach in treatment is ill-advised; thyrotoxic patients have a deep mistrust of parental figures and therefore a sympathetic and gentle approach is best.

Desmond O'Neill

963. **Hyperthyroidism Treated with Radioiodine**
W. H. BEIERWALTES and P. C. JOHNSON. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] 97, 393–402, April, 1956. 17 refs.

Between 1948 and 1955, 330 cases of thyrotoxicosis were treated with radioactive iodine (^{131}I) at the University of Michigan Hospital, Ann Arbor. These cases are here analysed in detail. The majority of the 82 patients with toxic nodular goitre were treated with ^{131}I because thyroidectomy was refused by the surgeon or by the patient (58%) or because preoperative preparation took more than 4 months (34%). Of the 248 patients with non-nodular goitre, 32% were so treated because thyroidectomy had previously been performed and 27% because they were over 40. Other reasons for this treatment included intolerance of antithyroid drugs and progressive exophthalmos.

Over the years the average initial dose of ^{131}I given has increased, but has now become stabilized at an average level of 12 mc. The maximum dose used in the treatment of nodular goitre was 45 mc. and of non-nodular goitre 25 mc., while the minimum dose in both groups was 4 mc. The size of the dose was determined empirically from the size of the goitre, the severity of the toxicosis, the general clinical state, and the proportion of a test dose of ^{131}I retained by the gland after 24 hours. No attempt is now made to treat the condition with a single large dose, up to 4 smaller doses being given at 3-monthly intervals.

At the time of the present review 71% of the patients with nodular and 78% of those with non-nodular goitre were judged to be free of thyrotoxicosis. There was some correlation between the size of the goitre and the total dose needed to achieve this end. Large nodular goitres required a larger dose than non-nodular goitres of comparable size; similarly nodular goitres recurrent after thyroidectomy required less than the average dose, whereas recurrences of the non-nodular type needed more. Resolution of the goitre was the rule, but the substernal extensions present in 8 cases did not change in size with treatment. The side-effects of the treatment were few; about 4 to 5% of patients had symptoms of mild thyroiditis, while 10% of the patients with nodular and 20% of those with non-nodular goitre became temporarily more toxic. In about one-third of the cases the degree of exophthalmos increased and in a similar proportion it decreased.

Thyroidectomy was carried out later in 8 cases for residual goitre. No carcinomatous change was found, nor was any relationship between the histological appearances and the dose of ^{131}I. Neither in these cases nor in 5 cases examined at necropsy were the histological changes of Hashimoto's disease seen, in contrast to the findings of Lindsay *et al.*

A. Gordon Beckett

964. **The Treatment of Patients with Toxic Goitre and Coexistent Pregnancy.** (Лечение больных токсическим зобом при сочетании его с беременностью)
E. E. BYKHOVSKAYA. *Проблемы Эндокринологии и Гортонотерапии* [*Probl. Endokr. Gormonoter.*] 2, 38–43, No. 2, March–April, 1956. 8 refs.

The author reviews and analyses reports published outside Russia of cases of pregnancy complicated by thyrotoxicosis and points out that there is no conclusive evidence that the unsuccessful outcome of some of these pregnancies was due to thiouracil therapy. Clinical details are given of 7 such cases which were investigated and treated at the Pavlov Institute of Physiology and the First Medical Institute, Leningrad. In 6 cases a primary diffuse toxic goitre was present and in one a toxic adenoma. At the time of admission the pregnancy was of less than 4 months' duration in 4 cases and more advanced in 3, and the management was determined accordingly. The 4 patients in the former group were treated by partial thyroidectomy after preparation with methylthiouracil and iodine; in each case the pregnancy proceeded normally after the operation and was followed by normal labour, all the mothers and children being well 19 to 24 months later. The 3 patients in the latter group, who were in the 26th, 35th, and 19th weeks of pregnancy respectively, were treated with methylthiou-

racil only, the drug being given subsequently if signs of a relapse appeared. All three pregnancies ended normally at term; the infants were healthy at birth and were developing normally when last seen 18 months to 4 years later.

The author concludes that when thyroidectomy is contraindicated methylthiouracil may safely be given in interrupted courses, right up to term if necessary. Particular care should be taken, however, not to induce hypothyroidism in the mother, as it is considered that it is maternal hypothyroidism and not the drug itself which is harmful to the foetus. Nevertheless it is advised that as thiouracil is excreted in the milk it should not be given to the mother during the period of breast-feeding.

Marcel Malden

ADRENAL GLANDS

965. **Addison's Disease and Pregnancy.** (Maladie d'Addison et grossesse)

L. DE GENNES, H. BRICAIRE, J. HAZARD, and E. BEAULIEU. *Presse médicale* [*Presse méd.*] **64**, 689–692, April 14, 1956. 13 refs.

From a review of the literature and from their own experience of 4 cases the authors conclude that normal pregnancy and delivery are not incompatible with the adrenal insufficiency of Addison's disease, although lactation is almost always deficient in such cases. In nearly all the recorded cases the infant has been healthy. There appear to be two critical periods, one at the beginning and one at the end of pregnancy, between which adrenal function seems to improve. The initial period is dangerous because of the serious effect that vomiting in early pregnancy may have on patients with adrenal insufficiency, and the terminal period is dangerous because of the risk of obstetric shock.

In the first of the authors' own cases a successful Caesarean section was carried out on a patient who had been known to have Addison's disease for 5 years and had been treated with deoxycortone by daily injection and later by implantation. The second patient had been treated with deoxycortone for 3 years, but then underwent a spontaneous remission. In spite of vomiting her condition did not deteriorate during pregnancy, but as a precaution she was given small amounts of deoxycortone for one month before and 3 weeks after a normal delivery. The third patient, who had had Addison's disease for 2 years, was treated with deoxycortone, cortisone, and salt, had a normal delivery, and was subsequently maintained on a reduced dosage. The fourth patient showed marked improvement during the second trimester in spite of very marked pigmentation. At this stage she required only 12·5 mg. of cortisone daily, whereas previously, and also after delivery, she needed 25 to 30 mg. Again labour and the puerperium were normal. The baby was healthy in all four cases.

The possible reasons for the apparent improvement in adrenal function during pregnancy in cases of Addison's disease are discussed at length. It is pointed out that not only does the urinary excretion of 17-ketosteroids increase nearly to normal, but the Thorn test result also may become positive. The authors consider that the production of adrenocortical steroids by the placenta is a more likely explanation than hypersecretion by the adrenal glands of the foetus.

T. D. Kellock

966. **Effects of Prolonged Cortisone Therapy on the Statural Growth, Skeletal Maturation and Metabolic Status of Children**

F. M. BLODGETT, L. BURGIN, D. IEZZONI, D. GRIBETZ, and N. B. TALBOT. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 636–641, April 5, 1956. 6 figs., 5 refs.

The effect of prolonged administration of cortisone on the growth pattern in 36 children was studied at Massachusetts General Hospital, Boston. The children were suffering from adrenocortical virilism (11), hypopituitarism (3), Addison's disease (2), and allergy (20), and were observed at intervals of 1 to 12 weeks. At each visit height and weight were recorded, a standard method of measurement being used, and radiographs were taken of the hands and wrists. Periodically electrocardiograms were recorded and the blood electrolyte concentration and urinary excretion of 17-ketosteroids determined.

Cortisone was given by mouth 2 or 3 times daily in a dosage varying from 4 to 60 mg. per square metre of body surface area per day, and within a few weeks of the start of treatment suppression of growth was observed. The dose causing growth suppression was 4 to 20 mg. per square metre of body surface per day in patients suffering from hypopituitarism, but in those with adrenocortical virilism a dosage of 30 to 50 mg. was necessary to cause reduction in growth of 20 to 70%. Patients with allergic disorders were in normal endocrine balance, and a dose of 60 mg. was needed for a reduction in growth rate of 20 to 100%. A compensatory growth spurt occurred in all patients except those with hypopituitarism when the dosage of cortisone was reduced. The authors tentatively conclude that the drug can be given for prolonged periods to growing children without necessarily altering the potential ultimate stature.

R. M. Todd

967. **The Influence of Cortisone upon Protein Metabolism**

P. R. CANNON, L. E. FRAZIER, and R. H. HUGHES. *A.M.A. Archives of Pathology* [*A.M.A. Arch. Path.*] **61**, 271–279, April, 1956. 3 figs., 18 refs.

In experiments carried out at the University of Chicago the authors endeavoured to determine whether the inhibitory action of cortisone on over-all protein synthesis in the intact rat was primarily catabolic or anti-anabolic, and whether this action could be counteracted by increasing the calorie intake or by administering B vitamins or ascorbic acid. It was shown first that with a diet deficient in protein the values for weight loss and nitrogen and potassium excretion were higher in cortisone-treated than in untreated animals. Secondly, it was demonstrated that cortisone interfered with the restoration of weight which usually occurred when a high-protein diet was given to protein-depleted animals. This action of cortisone was not affected by potassium

restriction, potassium supplements, or sodium supplements, and was associated with a slight negative balance of nitrogen and potassium. Moreover, it was unaffected by administration of rations reinforced with cyanocobalamin (vitamin B_{12}), ascorbic acid, or triple the amount of the vitamin mixture normally incorporated in the standard ration. However, an increase in the calorie intake, whether in the form of extra protein, carbohydrate, or fat, did cause an increase in weight, but carcase analyses revealed that this was mainly due to fat.

Using the term catabolism in a general sense, the authors conclude that in these experiments cortisone "acted catabolically".

[The dose of cortisone acetate (3 to 5 mg. per rat per day by mouth or 2·5 to 5 mg. per rat per day by subcutaneous injection) was high.] *Denis Abelson*

DIABETES

968. **Serum Lipids and Polysaccharides in Diabetes Mellitus**

D. Adlersberg, Chung-I Wang, H. Rifkin, J. Berkman, C. Ross, and C. Weinstein. *Diabetes* [*Diabetes*] **5**, 116–120, March–April, 1956. 4 figs., 28 refs.

The serum levels of total lipids, cholesterol, phospholipids, neutral fats, glucosamine, and protein-bound polysaccharides were estimated in healthy subjects, patients with uncomplicated diabetes, and diabetics with specific degenerative vascular disease. No differences were observed in any of these values between the healthy subjects and the patients with uncomplicated diabetes. In the diabetic patients with retinopathy but no evidence of renal involvement the serum levels of total lipids, neutral fats, glucosamine, and polysaccharides were significantly higher than in healthy controls. The values for all serum lipid fractions and also for glucosamine and polysaccharides were raised in diabetic patients with fully-developed retinal and renal involvement.

F. W. Chattaway

969. **Adrenalectomy for Vascular Disease of Diabetes**

J. M. Malins. *Lancet* [*Lancet*] **1**, 530–534, April 28, 1956. 32 refs.

The case reported by Poulsen (*Diabetes*, 1953, **2**, 7) of recovery from diabetic retinopathy following the onset of Simmonds's disease has aroused interest in the possibility of modifying diabetic vascular disease by reducing pituitary or adrenal function. At the General Hospital, Birmingham, total adrenalectomy was performed for vascular disease in 6 diabetic patients. All had increasing retinopathy; in addition 3 had albuminuria and hypertension and one had long-standing essential hypertension. One patient, already uraemic, died in renal failure 2 weeks after operation. In one patient both general health and retinopathy improved, with a return of visual acuity to normal, but in the remainder there was no significant change in the retinopathy or general health during a follow-up period of 5 to 16 months. The operation had no effect on albuminuria, hypertension, the management of the diabetes, or the insulin dosage. The author states that the fall in insulin requirements which had been observed by others was not seen in the present series of cases; this may have been due to the comparatively large maintenance dose of cortisone (50 mg.).

After discussing the general course of retinopathy and glomerulosclerosis, the author concludes that adrenalectomy is worth a further trial in patients who have rapidly advancing retinopathy or early established nephropathy. He considers that the operation is contraindicated in patients in renal failure with a blood urea level persistently above 70 mg. per 100 ml. and in those whose retinopathy has reached Ballantyne's Stage 4.

A. Gordon Beckett

970. **Ineffectiveness of Sulfonylureas in Alloxan Diabetic Rats**

I. A. Mirsky, G. Perisutti, and R. Jinks. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **91**, 475–477, March, 1956. 1 fig., 7 refs.

A great deal of interest has been aroused by reports that the oral administration of certain sulphonylureas will cause hypoglycaemia in animals and man and will reduce or even eliminate the need for exogenous insulin in many adult patients with diabetes mellitus. Reports of the effect of these substances on alloxan-diabetic animals, however, are conflicting, and in view of the importance of this point in determining the mode of action of the sulphonylureas in diabetes further investigations were undertaken at the University of Pittsburgh.

The administration by stomach tube of 100 mg. of 1-butyl-3-*p*-tolylsulphonylurea was found by the authors to produce a marked hypoglycaemic response in the normal rat, but not in the alloxan-diabetic rat. These observations are interpreted as evidence that the hypoglycaemic action of the sulphonylurea is related to an increased availability of insulin rather than to interference with the production of glucagon. Such an increase in insulin activity could be attributed either to an increased pancreatic production of the hormone or to a decreased rate of its destruction in the tissues. Previous work reported by the authors (*Metabolism*, 1956, **5**, 156; *Abstracts of World Medicine*, 1956, **20**, 137) has shown that tolylsulphonylurea is a non-competitive inhibitor of insulinase, the enzyme which catalyses the destruction of insulin, and it is therefore concluded that the inhibition of insulinase plays a role in the hypoglycaemic response to tolylsulphonylurea in the normal rat.

M. J. H. Smith

971. **Clinical Experiences with Carbutamide, an Orally Given Hypoglycemic Agent. Preliminary Report**

A. S. Ridolfo and W. R. Kirtley. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 1285–1288, April 14, 1956. 3 figs., 8 refs.

Clinical experience with the sulphonamide derivative carbutamide (*N*-butyl-*N'*-sulphanilylurea) in the treatment of diabetes is reported from the General Hospital, Indianapolis. Carbutamide when given by mouth is rapidly absorbed and slowly excreted. Its mode of

action in reducing hyperglycaemia is not yet established, but there is some evidence that it may act by selectively damaging the alpha cells of the pancreas and so suppressing glucagon production, or it may act as an insulinase inhibitor.

Toxicity is relatively low, although in some reported cases fever and skin eruptions occurred. Toxic symptoms were observed in only one of the 31 patients treated by the authors, and included mental clouding, a skin rash, and leucopenia, all of which cleared up when the drug was discontinued. Details are given of the results obtained in 11 hospital patients and 7 out-patients given carbutamide in a dosage of 1 to 6 g. daily. In 6 of the hospital patients, who had previously taken 10 to 60 units of insulin daily, no insulin was required, and in 3 others the dose of insulin necessary was significantly reduced. In the 2 remaining patients in this group 6 g. daily of carbutamide had no beneficial effect, both patients becoming acidotic.

From this experience and from reported results the authors came to the conclusion that factors predisposing to success with the drug are maturity, obesity, and relatively mild diabetes of short duration. With these factors in mind 7 out-patients were chosen for treatment; all responded well to the drug. Finally it is emphasized that carbutamide cannot be given in the treatment of acidosis or to young, unstable diabetics, and that attention must be paid to possible toxicity resulting from long-term administration. *T. D. Kellock*

972. **A Therapeutic Trial of "BZ 55" in Diabetes Mellitus.** (Essais de traitement du diabète sucré par le BZ 55)

R. Boulin. *Presse médicale* [*Presse méd.*] **64**, 643–645, April 7, 1956.

"BZ 55" (*N*-butyl-*N'*-sulphanilylurea; carbutamide one of the sulphonamides which has been shown to induce hypoglycaemia in normal animals and man, was used in the treatment of 15 patients aged 37 to 80 years with diabetes mellitus of moderate degree, 6 of whom had been receiving insulin in doses of 8 to 42 units daily, which was withdrawn on giving BZ 55. In one case the treatment had to be stopped because of increasing ketosis and in another because the blood sugar concentration did not fall; in the remaining 13 cases, however, it was possible with BZ 55 to reduce the blood sugar level, abolish glycosuria, and reduce the severity of an induced hyperglycaemia, although the glucose tolerance curve was still diabetic in type. There was no uniformity of blood sulphonamide concentration, indicating that absorption and excretion were very variable. There were no signs of renal or hepatic damage, agranulocytosis, or skin lesions during periods of administration ranging from 10 to 24 days.

The dosage suggested is 2·5 to 3 g. of BZ 55 on the first day, 1·5 g. on the second day, when the hypoglycaemia begins, and 1 g. or less on the following days. The drug has some cumulative action and the hypoglycaemia may persist for several days after stopping treatment. The author considers that BZ 55 may prove to be a useful drug in the management of diabetes mellitus, but he emphasizes that its administration will require the same strict supervision as that of insulin, that it in no way lessens the need for dietary control, and that, as with insulin, there is a danger of accidents and even catastrophes arising from the inadequate administration of the drug. *John Anderson*

973. **Study of a New Antidiabetic Sulphonamide. Clinical Indications and Dosage.** (Étude d'un nouveau sulfamide antidiabétique. Indications cliniques et posologie)

A. Ravina. *Presse médicale* [*Presse méd.*] **64**, 646–649, April 7, 1956. 6 refs.

Recent reports of the clinical use of the sulphonamide "BZ 55" (carbutamide) in diabetes mellitus are briefly reviewed, and treatment with this drug of 9 cases of diabetes with medical complications is described in detail. BZ 55 was found to reduce hyperglycaemia and glycosuria and is considered to be especially suitable for elderly, obese diabetics.

The author discusses the experimental evidence concerning the mode of action of the drug, and considers that the theory that it inhibits the α cells of the pancreas is supported by its observed clinical effects.

John Anderson

974. **Clinical Experience with the Oral Treatment of Diabetes.** (Klinische Erfahrungen mit peroraler Diabetes-Therapie)

J. Jacobi and M. Kammrath. *Ärztliche Wochenschrift* [*Ärztl. Wschr.*] **11**, 301–305, April 6, 1956. 7 figs., 14 refs.

The sulphonamide compound "BZ 55" (carbutamide) was used at the Marienkrankenhaus, Hamburg, in the treatment of 97 diabetic patients, 75 of whom were followed up for a sufficiently long time for the usefulness or otherwise of the new drug to be judged. Of the 75 patients, 12 were refractory to BZ 55, varying degrees of response being obtained in the remaining 63. Details of the treatment of 5 patients in whom the results were good are given; in each case insulin, previously required in doses up to 50 units daily, could safely be replaced by the new drug by mouth in doses of 1 to 1·5 g. daily, with which the blood sugar level was kept in check and glycosuria was either absent or negligible, though dietary measures had to be continued as before. The majority of patients responding well to the new drug were apparently of the sthenic type [though details of heights and weights are not given]. Combined treatment with insulin and BZ 55 has not yet been tried.

The drug is well tolerated, and even in an acid urine there is little risk of crystal formation. On resumption of insulin therapy, which is recommended at present in certain circumstances—for example, before an operation or in tuberculous patients under treatment with PAS or isoniazid—the patient's carbohydrate tolerance did not appear to have changed as a result of treatment with the new drug, that is, there was no evidence to suggest that it had an adverse effect on residual endogenous insulin production. *L. H. Worth*

The Rheumatic Diseases

975. **Studies in Rheumatic Fever**
J. A. JOHNSTON. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **91**, 250–267, March, 1956. 2 figs., 20 refs.

In 230 children with rheumatic fever seen between 1928 and 1949 at the Henry Ford Hospital, Detroit, there was a correlation between their nutritional status on admission (as judged by their position on the Wetzel grid) and the outcome. Of 164 with average nutrition or better the outcome was "satisfactory" (no carditis or no functional handicap) in 138, whereas of 66 with nutrition below average the outcome was satisfactory in only 40. The outcome was "unsatisfactory" (functional handicap or death) in 26 in each group. The outcome in children on an inadequate diet was somewhat less favourable than in those on a good diet.

Nitrogen and calcium balance studies carried out on 30 children during treatment with cortisone or corticotrophin showed large losses of nitrogen during the first 10 days, but the effect on calcium balance was not consistent. On hormone withdrawal there was a rapid rebound of storage of nitrogen. Prolonged bed rest adversely influenced the retention of nitrogen and calcium, but even very moderate degrees of activity offset this tendency. On a regimen of combined cortisone, salicylates, and ascorbic acid significantly better results were obtained than in a series of cases treated in the preceding 10 years, but a general decline in the severity of this disease may have contributed to this effect. *John Lorber*

976. **The Clearing Factor in Rheumatic Fever.** (Le facteur d'éclaircissement dans la maladie de Bouillaud)
H. KAUFMANN, G. DOURDOU, D. LYON, J. PAYOT, and P. ISORNI. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **49**, 147–152, Feb., 1956. 2 refs.

The absence of a lipid-clearing factor in the plasma of patients suffering from rheumatic fever has previously been pointed out by the first-named author (*Presse méd.*, 1955, **63**, 1045). In this paper from the Hôpital de Versailles further details of the potential clinical value of this phenomenon are presented with reference to the investigation of 36 cases of acute rheumatic fever with joint involvement, the clearing factor being sought at the beginning of an acute attack, on the disappearance of physical signs, and during relapse. At the same time the concurrent changes in the erythrocyte sedimentation rate (E.S.R.), leucocyte count, antistreptolysin-O titre, and in the electrophoretic pattern of the plasma proteins were determined.

The clearing factor was found to disappear in all cases examined during the acute phase of the illness, and to reappear as soon as this phase began to subside. This process was more rapid in patients being treated with cortisone than in those receiving salicylates and aspirin. In many cases the clearing factor disappeared before increases in the E.S.R., leucocyte count, or the plasma α-globulin level were detectable. Similarly the reappearance of the factor was noted even before the onset of clinical improvement, and before any other changes in the laboratory tests, this finding being again particularly marked in patients receiving cortisone. During relapse a similar precocity of changes in the clearing factor was noted; thus in 2 cases in relapse the factor disappeared on the first day, whereas changes in the E.S.R. and protein electrophoretic pattern only appeared on the third day. In some cases the disappearance of the clearing factor was noted as early as 24 hours before the clinical appearance of a relapse.

Although the test for the lipid-clearing factor is not specific for rheumatic fever—similar changes having been noted in some types of anaemia, acute pulmonary states, and certain neurological and endocrine conditions [not specified]—the authors suggest that as the test is simple and useful diagnostically it should prove of value as a routine measure once the practical difficulty of providing a lipid substrate which will give consistent results can be overcome. *P. I. Reed*

977. **Results of Cortisone and ACTH Treatment of Rheumatic Fever**
M. S. HECHT, W. E. SHELDEN, A. NOLKE, D. HOFSTRA, and E. WEST. *Journal of Pediatrics* [*J. Pediat.*] **48**, 300–307, March, 1956. 16 refs.

Cortisone and ACTH were given in the treatment of 122 cases of rheumatic fever admitted to the Children's Hospital of Michigan, Detroit, between April, 1950, and September, 1953. All the patients, who were under 12 years of age, were followed up for at least one year after cessation of treatment. Details are given of the dosages of the drugs and of other forms of therapy employed. Some signs of the Cushing syndrome were observed in most cases during treatment and transient glycosuria and hypertension were noted in a few. In some cases chicken pox, mumps, and measles developed, but these diseases ran their usual courses. The duration of treatment did not exceed 12 weeks, except in 3 cases. In 24 cases valvular lesions disappeared. The size of the heart decreased in 25 cases and increased in 7. There were 3 deaths in the series, and in 16 cases there was a recurrence of rheumatic activity.

These results were compared with those obtained in a similar group of cases of rheumatic fever admitted to the same hospital between December, 1946, and April, 1950, and treated with salicylates. Signs of valvular lesions disappeared in only 3 cases in the latter series and there were 15 deaths. It is concluded that although hormone therapy does not cure rheumatic fever, it is useful in suppressing the inflammatory reactions which occur during rheumatic activity. *Kathleen M. Lawther*

978. **The Relationship of Sydenham's Chorea to Infection with Group A Streptococci**
A. TARANTA and G. H. STOLLERMAN. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 170–175, Feb., 1956. 3 figs., 11 refs.

The relationship between Sydenham's chorea and streptococcal infections was studied by analysing the case histories of patients observed during a first attack of chorea under conditions in which streptococcal infection could be controlled and the serum antibody titre determined.

Of 10 patients with "pure" chorea who were seen within 5 months of the onset of choreiform activity, 8 had a serum antistreptolysin-O (ASO) titre of more than 200 units per ml.; of the 2 remaining patients one had a serum antihyaluronidase titre of 300 units per ml., while the serum of the other showed no increase in the titre of the three streptococcal antibodies studied. In another series 27 out of 41 patients had serum ASO titres of more than 200 units per ml. It appeared that the earlier the patient was tested after the onset of chorea, the higher was the serum ASO titre, although in general the titre in these cases was rather lower than that observed in acute rheumatic fever. In those cases in which chorea is associated with other manifestations of acute rheumatism it tends to follow them after an interval as long as 7 months, with no evidence of a fresh streptococcal infection during that time, and by the time chorea develops the serum content of antistreptococcal antibodies may have fallen to normal.

The authors consider it reasonable to assume that the same relatively long latent period intervenes between the streptococcal infection and the onset of chorea when it occurs as an isolated phenomenon, and suggest that this may explain the lack of immunological evidence of streptococcal infection in some cases of "pure" chorea.
G. Loewi

979. **Liver Function Tests in Rheumatoid Arthritis**
P. W. DARBY. *Journal of Clinical Pathology* [*J. clin. Path.*] **9**, 153–156, May, 1956. 2 figs., 35 refs.

Numerous attempts have been made to demonstrate an impairment of liver function in association with rheumatoid arthritis. The present author's contribution is particularly concerned with the results of the "bromsulphalein" retention test, the coproporphyrin urinary excretion test, and various flocculation tests and with the serum bilirubin level and urinary urobilinogen excretion in this disease. The tests were carried out at the Westminster Hospital, London, on 50 cases of rheumatoid arthritis and a control series of 45 patients with other diseases, the groups being similar in age and sex distribution and in the proportion of ambulant cases which they contained.

In 11 out of 47 cases of rheumatoid arthritis dye retention was 10% or more 30 minutes after an intravenous injection of 5 mg. of bromsulphalein per kg. body weight, whereas only in 2 of the 44 control subjects tested was there retention to this degree. This difference is shown to be statistically significant. The urinary coproporphyrin excretion was studied because of its sensitivity as an index of liver function. The coproporphyrin content of afternoon collections of urine over a 2-hour period from 26 healthy subjects showed the normal value to be less than 20 μg. Of 49 patients with rheumatoid arthritis, 15 showed an excretion in excess of this value, compared with only 2 of the 41 in the control group. Statistical analysis again shows this difference to be highly significant. The serum bilirubin and urinary urobilinogen levels were within the normal range in both groups and the results of the flocculation tests were inconclusive. These results are held to confirm that in a proportion of cases of rheumatoid arthritis (between one-quarter and one-third of the present series) there is evidence of some impairment of liver function. The degree of impairment in such cases could not be correlated with the severity or duration of the rheumatoid condition, nor was impairment less common in treated than in untreated cases. [While not entirely consistent with the findings reported in the very many other papers on this subject, the conclusions reached in this paper seem to be derived from a very fair assessment of the facts observed.] *Harry Coke*

980. **The Clinical Significance of Histological Amyloid in Rheumatoid Arthritis.** [In English]
V. LAINE, P. MÄKINEN, G. L. MÄKINEN, T. HOLOPAINEN, and E. SAIRANEN. *Acta rheumatologica Scandinavica* [*Acta rheum. scand.*] **1**, 257–261, 1956. 1 ref.

In a previous report from the Hospital of the Rheumatism Foundation, Heinola, Finland, the authors described the occurrence of amyloid-like material in 50% of biopsy specimens of various tissues (but mainly the skin) in patients suffering from rheumatoid arthritis. They now report an attempt to correlate the biopsy findings with the clinical features in 100 unselected cases of rheumatoid arthritis, 37 in men and 63 in women. The degree of the amyloid change tended to be more pronounced in severe cases of rheumatoid arthritis, but no definite correlation was obtained with sex, age, or duration of the disease. *R. E. Tunbridge*

981. **Clinical Evaluation of Prolonged ACTH and Cortisone Therapy in 114 Cases of Rheumatoid Arthritis.** [In English]
J. H. SOLEM and O. RÖMCKE. *Acta rheumatologica Scandinavica* [*Acta rheum. scand.*] **1**, 243–249, 1956. 10 refs.

A report is presented, from Drammen Hospital, Drammen, Norway, of the results of a 3½-year study of 208 patients with rheumatoid arthritis, of whom 114 were found suitable for prolonged hormone therapy. ACTH (corticotrophin) was given by injection in the long-acting gel form in a dose of 20 units 3 times a week. Other patients received cortisone, 50 mg. per day, the longest period of treatment up to the end of the survey being 25 months. There was satisfactory improvement in 30% of the patients; the usual side-effects were noted, but none were fatal. The authors stress that this type of long-term therapy is suitable for only a small proportion of patients—in the present series it amounted to 16%. *G. S. Crockett*

Physical Medicine

982. **Increased Ohmic Resistance of the Skin in Head's Zones in Diseases of Various Abdominal Organs.** (Электрокожная сопротивляемость и чувствительность в зонах Захарьина-Геда при заболевании органов брюшной полости)
M. B. DUNAEVSKAYA. *Советская Медицина* [*Sovetsk. Med.*] 51–61, No. 3, March, 1956. 8 figs., 1 ref.

The author confirms observations of Head that in affections of the various organs of the abdominal cavity, such as the stomach, pancreas, gall-bladder, or adrenal glands, the site of the area of referred increased tenderness in the skin is specific and constant. In doubtful cases, by the method of "galvano-palpation", the affected organ can be identified by the finding of increased ohmic resistance of the skin in the area of maximum referred pain.

It is claimed that this method permits early recognition not only of the diseased organ, but also of the various sequelae which may follow an inflammatory affection of that organ; it also allows of the differentiation between gastric and duodenal ulcer. In the author's protracted cases leading to the so-called gastro-hepato-pancreatico-duodenal syndrome it became possible to discover additional, well-defined areas of increased ohmic resistance of the skin characteristic of involvement of the liver and pancreas. However, the author stresses the necessity of correlating the results of this method with the other clinical findings. *A. Orley*

983. **Clearance of Radioactive Sodium from the Knee Joint**
R. HARRIS and J. B. MILLARD. *Clinical Science* [*Clin. Sci.*] **15**, 9–15, 1956. 6 figs., 5 refs.

At the Devonshire Royal Hospital, Buxton, Derbyshire, the authors have carried out a quantitative study of the local circulation in the knee-joint of 20 healthy subjects by determining the clearance of radioactive sodium (^{24}Na) measured with unshielded scintillation counters at one-minute intervals up to one hour after the injection of 5 to 10 microcuries of ^{24}Na in isotonic saline solution into the knee joint. The results were plotted semi-logarithmically against time and showed that the clearance from the joint was exponential; the mean clearance constant (K) in 23 tests was found to be $0{\cdot}050 \pm 0{\cdot}021$.

Arterial occlusion in the thigh by means of a cuff at a pressure of 200 mm. Hg completely inhibited clearance, while venous occlusion at a pressure of 60 mm. Hg effected a significant decrease in the rate. Light, non-weight-bearing exercise was followed by a decrease in clearance, while heating of the knee-joint by short-wave diathermy, producing an elevation of the intra-articular temperature of 3° to 6° C., increased the rate of clearance by 100%. The authors consider that the technique and the method of assessment by the clearance constant give accurate and sensitive results and moreover are suitable for the study of local circulatory changes within the knee-joint. *Harry Coke*

984. **Physical Medicine in the Treatment of Peripheral Vascular Disease of the Obliterative Thromboangiitis Type.** (Лечебная физическая культура при заболевании периферических сосудов типа облитерирующего тромбангиита)
D. N. VILENSKII. *Вопросы Курортологии, Физиотерапии, и Лечебной Физической Культуры* [*Vop. Kurort. Fizioter.*] 51–54, No. 1, Jan.–March, 1956.

In this discussion of the physical medical treatment of obliterative peripheral vascular disease the author's main contention is that although exercise of the muscles of the affected limb results in a local increase of blood flow, as in the normal limb, movements of other extremities tends to produce a vasospasm in the affected limb at rest. Therefore exercise of the affected limb should be so devised as to maintain immobility of the other limbs. Deep breathing was found to have a beneficial effect on circulation in the affected parts, while relaxation exercises helped to combat vascular spasm. [It should be noted that these results have been obtained in the treatment of only 8 patients.]

Capillary abnormalities in the affected parts were studied by means of capillaroscopy. The clotting and bleeding times of the blood from the affected extremities were found to be significantly reduced as compared with those of blood from the unaffected extremities of the same patients. *A. Swan*

985. **Active Immobilization of Joints in Rheumatoid Arthritis**
M. KELLY. *New Zealand Medical Journal* [*N.Z. med. J.*] **55**, 11–14, Feb., 1956. 4 figs., 4 refs.

It is pointed out that rheumatoid arthritis is a disease of movement and that if there were no movement there would be no disease. Control of movement, therefore, becomes the most important of all therapeutic measures in the management of cases of rheumatoid arthritis. The author advocates active immobilization by splinting a painful joint and allowing the patient to use the limb. The wrists and elbows may be immobilized in plaster for approximately 4 weeks, then gradually mobilized. The shoulder should be immobilized by strapping the arm and forearm to the chest wall for 3 weeks. For the knee immobilization in a band caliper for 4 weeks is preferred, walking being encouraged. Manipulation under anaesthesia may be necessary to correct a flexion deformity of the knee; this is followed by immobilization in a splint.

The author emphasizes that immobilization by splinting for a few weeks is not followed by ankylosis if the joint cartilage is intact. Immobilization allows the

swelling to subside and facilitates the return of a good range of movement. If the cartilage is disorganized a stable arthrodesis is a good result. *J. B. Millard*

986. **Physiological Effects of Simultaneous Static and Dynamic Exercise**

F. A. HELLEBRANDT, S. J. HOUTZ, D. E. HOCKMAN, and M. J. PARTRIDGE. *American Journal of Physical Medicine* [*Amer. J. phys. Med.*] **35**, 106–117, April, 1956. 8 figs., 7 refs.

Repetitive exercise of a limb is associated with a progressive decrease in functional capacity which is proportional to the severity of effort, and it has been shown that simultaneous activity of the homologous muscle groups of the contralateral limb has a facilitatory effect on the limb exercised. The present investigation was carried out at the Research and Educational Hospitals of the University of Illinois, Chicago, on 9 healthy adults (5 males) to study the effects of simultaneous static and dynamic exercise. All experiments were carried out with the wrist ergograph, the exercise being wrist extension with the forearm in pronation; action potentials were picked up by surface electrodes and recorded on an ink-writing apparatus after appropriate amplification.

Two types of exercise were employed: (1) single bouts of repetitive unilateral activity with loads which sufficed to produce complete exhaustion in 30 to 120 seconds; and (2) repeated bouts against lesser resistance, each bout lasting one-half minute with a rest-pause of the same duration between bouts; the end-point of volitional effort was usually reached in 10 or 12 successive bouts of 25 contractions each. Work output during dynamic exercise was measured by multiplying the distance through which the load moved by the magnitude of the resistance. Static exercise was performed by holding the ergographic load by sustained wrist extension. In the single-bout experiments, each limb first performed independently, then after an appropriate rest-period both exercised synchronously; but if one failed before the other the stronger continued to the point of exhaustion. When repeated bouts of dynamic exercise were performed, static exercise by the contralateral limb was introduced during alternate bouts. Even with training, these experiments imposed considerable stress on the subjects and the Valsalva phenomenon, for instance, became a complicating factor in the interpretation of the results.

In all, 165 experiments were performed, from which the conclusion is reached that simultaneous static and dynamic work is mutually facilitatory (in the trained subject) and that the degree of facilitation is related to the severity of the effort. It was noted that when rhythmical dynamic activity is performed by the left hand of a right-handed subject and static exercise by the right hand the rhythm of the dynamic activity was communicated to the right hand and influenced the form of the static ergogram, but when the procedure was reversed this transmission was much less obvious, the left hand in this case acting in the normal capacity as the holding hand. The practical implications of these observations, particularly in relation to the exercise techniques available to the physiotherapist dealing with muscle re-education after lesions of the central nervous system, are obvious. *D. Preiskel*

987. **The Application of Progressive Resistance Exercise in Physiotherapy**

I. J. MACQUEEN. *Physiotherapy* [*Physiotherapy*] **42**, 83–93, April, 1956. 10 figs., 17 refs.

Writing from the Nuffield Orthopaedic Centre, Oxford, the author states that to make progressive resistance exercise effective in building muscle it is necessary to find the correct combination of resistance and number and frequency of repetitions. Resistance is essential for an increase in the bulk and power of muscle, for mere repetition of free exercises alone does not achieve this. Formerly the most popular plan was to increase the resistance (that is, the weight lifted) between each set of exercise repetitions until a maximum weight had been achieved, but this has now been largely superseded by the use of a constant 10-repetition maximum for every set of repetitions. Professional weight-lifters start with maximum sets of 10 repetitions and then increase the weight until finally it can be lifted only once. The same technique has been found by the author to be of great value in the training of athletes. It is his opinion that in therapeutic " resisted exercise " it is important to combine the development both of muscle bulk and of muscle strength, and this has been confirmed by animal experiments which are briefly described. Thus in a programme of progressive resistance exercise the work undertaken by the patient at any one session must never be less, but at least equal to or preferably greater than that undertaken at the previous session.

The author then goes on to consider the applications of progressive resistance exercise. He finds it has a preventive part to play in maintaining fitness and efficiency and in protecting joints from injury by reducing the risks arising from instability. After fractures progressive resistance exercises improve the circulation and help neuromuscular reduction. He points out that Trueta's work on osteoarthritis suggests that the logical treatment of early osteoarthritis of the hip is to subject every segment of the femoral head to strong intermittent pressure in order to encourage imbibition of the synovial fluid and maintain the health of the articular cartilage. In neurological conditions, especially in poliomyelitis, progressive resistance exercise has one of its most useful applications; it may be started as soon as soreness has disappeared. In muscles which have not yet recovered antigravity strength, underwater progressive resistance exercise should be carried out. The author advocates the Kabat–Kaiser proprioceptive facilitation technique, combined with progressive resistance exercise. " Cheating ", that is, by bringing neighbouring muscles into play, can be helpful in progressive resistance exercise if at the same time it adds to the power of the muscle which is primarily being exercised. The technique of treatment on an inclined plane is described in some detail. Finally, the author reminds us that no muscle, healthy or diseased, has ever been developed except by hard work. *W. Tegner*

Neurology and Neurosurgery

988. **Spontaneous Spinal Subarachnoid Haemorrhage**
R. A. HENSON and P. B. CROFT. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **25**, 53–66, Jan., 1956 [received April, 1956]. 4 figs., 29 refs.

The clinical features of spontaneous subarachnoid haemorrhage of spinal origin, based on 7 cases which came under the authors' care and on the records of 5 others in which haemorrhage was discovered at necropsy, are analysed in this paper from the London Hospital and the Maida Vale Hospital for Nervous Diseases. In the authors' cases acute agonizing pain in the back was the first symptom, and was often followed by bilateral sciatica. Headache and vomiting then occurred in all cases, indicating an extension of the extravasated blood to the cranium. Signs of spinal-cord involvement were frequently noted, but the authors state that these were slight in their patients " in spite of the size of the causal lesions ". Haematomyelia was not encountered.

The cause of the haemorrhage was known in 3 of the authors' 7 cases, being a spinal angioma in 2 and rupture of an aneurysm of the posterior spinal artery in one case. It was considered probable that angiomata were present in 3 of the remaining 4 cases. Of the 5 cases discovered at necropsy, periarteritis nodosa was present in 2 and spina bifida and meningocele in one. In this last case a mycotic aneurysm in the lumbar sac had ruptured. Of the 7 patients in the present series 2 died, the remainder making a good recovery. The authors attribute the relatively good prognosis to the absence of a complicating haematomyelia.
Fergus R. Ferguson

989. **A Clinical Trial of Benactyzine Hydrochloride (" Suavitil ") as a Physical Relaxant**
A. COADY and E. C. O. JEWESBURY. *British Medical Journal* [*Brit. med. J.*] **1**, 485–487, March 3, 1956. 7 refs.

The authors treated 80 patients with a variety of disorders attending neurological clinics at the Royal Northern Hospital, London, Chase Farm Hospital, Enfield, and the Luton and Dunstable Hospital with benactyzine hydrochloride (" suavitil ") in order to investigate its effect on muscular rigidity and muscular spasm of organic or psychogenic origin. Doses of 2 mg. 3 times daily by mouth were given to 72 patients for 2 weeks, the course being extended to 4 weeks in some cases and a further period of 2 weeks' treatment with 3 or 4 mg. 3 times daily being given in a few. The remaining 8 patients received 4 mg. 3 times daily for one week only. Control tablets were given before or after the benactyzine to 53 of the patients, of whom 26 reported improvement with benactyzine and 24 with the control. No effect on muscle tone or rigidity was noted. Of 29 patients with disseminated sclerosis, 10 reported diminution or disappearance of flexor spasms and jerking of the legs in bed at night, but in 5 of these cases the improvement persisted when the control tablets were substituted.

Of the 72 patients given 2-mg. doses, 29 reported side-effects such as apathy and abnormal sensations in the limbs. Dizziness occurred in 13 patients. All the 8 patients given 4-mg. doses reported side-effects. Doses of 2 mg. given before meals to healthy medical observers gave rise to a " far-away " feeling, a sensation of relaxation or detachment approaching depersonalization, apathy, difficulty in concentration, and hesitancy in speech. Doses increasing from 2 to 15 mg. produced increasing blockage of thought; the subject wanted to lie down and showed a striking flatness of affect. These effects began about 20 minutes after ingestion of the drug and lasted for about 1½ hours, and it is advised that patients should be warned not to drive motor vehicles while under treatment with benactyzine. In view of these side-effects the value of the drug in the treatment of non-psychiatric cases would seem to be limited.

Both subcutaneous and oral administration of benactyzine caused suppression of normal activity in the electroencephalogram, this becoming intermittent as the effect wore off. No such effect is produced by chlorpromazine, reserpine, or other compounds derived from antihistamine drugs.
G. de M. Rudolf

DIAGNOSTIC METHODS

990. **Sleep as a General Activation Procedure in Electroencephalography**
D. SILVERMAN. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **8**, 317–324, May, 1956. 8 figs., 19 refs.

Attempts were made to obtain sleep records from 1,000 patients on whom routine electroencephalography was carried out at the Graduate Hospital of the University of Pennsylvania, Philadelphia. Sleep was induced with " dormison " (methylpentynol), 750 mg. for adults and 250 to 500 mg. for children, which was followed by ¾ to 1½ grain (50 to 100 mg.) of " seconal " (quinalbarbitone) 45 minutes later if necessary. Successful sleep records were obtained in 797 cases, while a further 84 patients became drowsy.

Abnormalities of diagnostic value were recorded in 201 cases; in 123 of these the changes observed during sleep confirmed or amplified those which were evident in the waking record or during hyperventilation or photic stimulation, but in 78 cases significant changes occurred only during sleep. The highest proportion of abnormalities was found in the records of individuals with epilepsy or the post-traumatic syndrome, the sleep record being only rarely of value in patients with cerebral tumour or with vascular, degenerative, or psychiatric disorders.

[The author does not clearly distinguish between the different forms of epilepsy in this study; many workers are agreed that sleep is particularly valuable in eliciting the characteristic discharges of temporal-lobe epilepsy.]
John N. Walton

991. **EEG Activation with Chloralosane**
R. R. MONROE, R. G. HEATH, W. MILLER, and C. FONTANA. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **8**, 279–287, May, 1956. 4 figs., 12 refs.

The authors, working at the Charity Hospital (Tulane University School of Medicine), New Orleans, have investigated the effects of hyoscine (scopolamine) and α chloralose (" chloralosane ") upon the electroencephalogram (EEG) of 31 patients suffering from a variety of psychiatric disorders, including 14 psychotic individuals. After a period of routine recording, including 3 minutes of hyperventilation, 500 mg. of chloralose and 0·5 mg. of hyoscine were given by mouth. The recordings were continued for at least 2 hours, with hyperventilation every 15 minutes. The findings in these patients were compared with those in 15 normal control individuals and in 8 patients (6 with schizophrenia, 1 with episodic psychosis, 1 with cerebral metastases) with implanted intracerebral electrodes, all of whom were subjected to the same procedure.

In all but 3 of the psychiatric patients there was some activation of the EEG by the drugs, whereas this occurred in only 4 of the normal controls. The findings in the patients with intracerebral electrodes did not reveal any evidence of subcortical activation occurring consistently before the involvement of the cortical areas. Activation, which usually started within the first hour after administration of the drugs and reached a maximum during the second, consisted in the appearance of mixed theta and delta activity which was sometimes continuous, sometimes paroxysmal; it tended to be focal at first and to become generalized later. Sometimes spikes or sharp waves were seen and previous symptoms or abnormalities of behaviour were increased. As only 7 of the 32 individuals showing activation had a history of seizures, the authors conclude that it would be dangerous to diagnose epilepsy on the basis of EEG abnormalities evoked in this way. The technique may, however, prove to be useful in the identification of a specific group of behaviour disorders. *John N. Walton*

992. **EEG Findings following Intravenous Injection of Diphenhydramine Hydrochloride (Benadryl)**
R. DIAZ-GUERRERO, R. FEINSTEIN, and J. S. GOTTLIEB. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **8**, 299–306, May, 1956. 5 figs., 17 refs.

The authors have studied the changes induced in the electroencephalogram (EEG) by the intravenous injection of " benadryl " (diphenhydramine) in 14 control subjects and in 50 patients with seizures. Of the latter, 21 suffered from seizures of unknown aetiology, 8 from seizures following a head injury, 6 from behaviour disturbances, and 5 from hysteria or syncopal attacks, while 10 were undergoing electric convulsion therapy and had had 10 to 15 treatments. All the patients had discontinued any anticonvulsant medication 72 hours before the test and were fasting. A preliminary tracing was recorded, with photic stimulation and with hyperventilation, and the diphenhydramine was then injected intravenously, 10 mg. being given every 15 seconds up to a total of 60 to 100 mg. and the recording being continued for at least 30 minutes after completion of the injection.

The drug had no effect upon the records of the normal control subjects unless they became drowsy, when sleep activity appeared. Where paroxysmal diffuse slow activity was present initially this was markedly reduced after the injection. However, focal spike or spike-and-wave activity was greatly increased after the injection, while discharges of this nature appeared in some records which had previously been normal. The authors suggest that the cerebral mechanisms responsible for paroxysmal slow activity may be stimulated by diphenhydramine to work more rapidly, this accounting for the reduction of slow activity, while similar stimulation increases focal spike or sharp wave discharges. It would thus appear that diphenhydramine (or other antihistamine drugs) may sometimes be of value for activation of the EEG in patients who are believed to be suffering from focal epilepsy. *John N. Walton*

BRAIN AND MENINGES

993. **An Aetiological, Clinical, and Therapeutic Study of " Pseudotumor Cerebri ".** " Pseudotumor cerebri ". Ätiologie, Klinik und Therapie)
E. KETZ. *Deutsche Zeitschrift für Nervenheilkunde* [*Dtsch. Z. Nervenheilk.*] **174**, 331–356, 1956. 4 figs., bibliography.

The author reports 17 examples of " pseudotumor cerebri " occurring among a total of 1,027 cases of cerebral tumour seen during a period of 8 years at the Neurological and Neurosurgical Clinic of the Free University of Berlin, and discusses the aetiology, clinical features, and treatment of this condition in conjunction with a review of the relevant literature of the last 50 years. He considers that the use of the term " pseudotumor cerebri " should be restricted to the syndrome characterized by raised intracranial pressure and papilloedema, with or without focal signs, arising as a result of a localized encephalitis without abscess formation, or of local or generalized cerebral oedema either due to a vascular disorder or of which the pathogenesis remains obscure. All other conditions which may simulate a tumour of the brain should, in his opinion, be distinguishable by modern diagnostic methods, whereas in the conditions mentioned above the diagnosis is often indicated only by the course of the disease. Cases illustrative of each of the three types of pathogenesis are described, together with the results of their investigation by angiography, encephalography, and electroencephalography. Of 8 cases of the inflammatory (encephalitic) type, 6 resolved completely and in 2 there were minor

residual mental changes; biopsy of the brain in 4 cases showed inflammatory changes. Of the 3 patients with localized cerebral oedema of vascular origin, 2 had arterial hypertension and the third had undergone ligation of the jugular veins one year previously during treatment for carcinoma of the larynx with cervical metastases. Of these, 2 recovered completely and one was left with slight mental changes. Of 6 patients with cerebral oedema of undetermined aetiology, 3 recovered fully and 3 died. One of those who recovered was 3 months pregnant at the onset and recovered rapidly after termination of the pregnancy.

Once the condition is diagnosed treatment should be conservative, but cranial decompression may be necessary for diagnostic purposes or to relieve a rapidly increasing intracranial pressure which is threatening the sight or the vital centres. In hypertensive cases measures should be taken to reduce the blood pressure. Estimations of the cerebral blood flow were found to be helpful as a guide to improvement, while changes in the electroencephalogram, when present, tended to disappear early in those cases in which there was subsequent recovery.

J. B. Stanton

994. **The Early Diagnosis of Basilar Impression and Assimilation of the Atlas from the Clinical Picture.** (Frühdiagnose basilarer Impression und Atlasassimilation aus dem klinischen Erscheinungsbild)

H. Dieckmann. *Deutsche Zeitschrift für Nervenheilkunde* [*Dtsch. Z. Nervenheilk.*] **174**, 525–540, 1956. 4 figs., bibliography.

From the City Hospital, Dortmund, 6 cases of basilar impression (platybasia) seen within one year are described and illustrated, and discussed together with other cases reported in the literature. Alterations in the posture of the head resulting from anomalies of the cervical spine, nystagmus, cervical and occipital pain, and involvement of the lower cranial nerves—particularly unilateral atrophy of the tongue—are features which should bring this condition to mind in the early stages. Confirmation is by careful radiography and tomography; the interpretation of the films is described. The author stresses that platybasia, when primary, often exists in conjunction with other congenital malformations, such as syringomyelia (as in 3 of the present cases) or Arnold–Chiari malformation, and that this increases the difficulties of diagnosis.

J. B. Stanton

995. **Subdural Collections of Fluid in Infants and Children. II. Study with Radioactive Sodium Phosphate (P-32)**

R. M. N. Crosby and R. E. Bauer. *Journal of Neurosurgery* [*J. Neurosurg.*] **13**, 140–144, March, 1956. 1 fig., 1 ref.

The investigation described in this paper from the University of Maryland School of Medicine, Baltimore, was designed to assess the degree of encapsulation of subdural collections of fluid in infants and children. Assessment of encapsulation normally requires an exploratory trephine opening in order to decide whether operative removal of the capsule is necessary. The present authors hoped to avoid this by adopting the following procedure. An intravenous injection of 1 to 200 μc. of radioactive phosphorous (^{32}P) in 1 to 2 ml. of fluid was given to patients with an open fontanelle and a subdural collection of fluid requiring repeated aspiration. Samples of whole blood and subdural fluid were taken 3 hours later. The subdural activity was expressed as a number obtained by the following equation from the counts per minute (C.P.M.):

$$\frac{\text{C.P.M. per ml. of subdural fluid}}{\text{C.P.M. per ml. of plasma}} \times 100$$

Peak concentration, which was determined in one case by continuous aspiration, occurred 3 hours after injection of ^{32}P. Results of 35 trials in 29 cases are given in a table. In cases in which subdural collections of fluid were associated with nutritional and metabolic disorders a value of 15 or more by this method indicated encapsulation. In the traumatic and inflammatory types of case a value of 130 or more was a definite indication of encapsulation.

Brodie Hughes

996. **The Syndrome of Apractognosia Due to Lesions of the Minor Cerebral Hemisphere**

H. Hécaen, W. Penfield, C. Bertrand, and R. Malmo. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Arch. Neurol. Psychiat.*] **75**, 400–434, April, 1956. 23 figs., 17 refs.

This paper from the Montreal Neurological Institute and McGill University discusses the apractognostic syndrome produced by lesions of the minor (non-dominant) parietal cortex. A detailed study was made of 17 patients who had undergone well-localized parietal or parieto-temporo-occipital excisions for focal epilepsy, the right hemisphere being affected in 15 right-handed patients and the left in 2 who were left-handed. Search was made for defects of: praxis (apraxia for dressing, ideational, ideomotor, and constructive apraxia); body scheme (awareness of the body-half, right and left orientation, finger gnosis, and autotopognosis); spatial gnosis (spatial orientation, topographical relationships, notion of distances and depth, map orientation); visual gnosis for images and objects with tachystoscopic examinations, perception of visual coordinates (subjective horizontal and vertical); calculation and counting, time and rhythm appreciation; and oculomotor movements, with graphic recordings. In some cases psychological examinations were made.

Apractognostic disturbances were found in 10 of the 17 cases, though one was discarded because of a low intelligence rating, and 5 of these are reported in full detail as representative of the syndrome. In addition to body-scheme disturbances of the anosognosic type there were visuoconstructive disabilities, apraxia for dressing, difficulties in spatial orientation, and alterations of visual coordinates, while loss of topographical memory was also a probable constituent of the syndrome, although a disputable one.

The authors point out that " there is a strange difference, which is not easily understood, between the functions of the two parietal lobes. A lesion in the

parietal area of the dominant hemisphere produces bilateral body-scheme disorders, either localized to the fingers (finger agnosia) or generalized (autotopognosia). On the other hand, a lesion in the minor parietal area disturbs the body scheme unilaterally".

[This paper should be read in the original.]

J. MacD. Holmes

997. **Syndrome of the Jugular Foramen. A Syndrome Resulting from Neoplasms of the Posterior Fossa**
B. L. CRUE, D. B. FRESHWATER, C. H. SHELDEN, L. G. HUNNICUTT, and F. JOHNSON. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] 63, 384–391, April, 1956. 10 figs., 7 refs.

The typical signs of neoplasm in the posterior fossa are damage to the 9th, 10th, and 11th cranial nerves; the 12th nerve, some distance off in its own canal, is less likely to be affected. As the internal auditory meatus is immediately above the jugular foramen, the 7th and 8th cranial nerves are also often damaged. In glomus jugulare tumours of the jugular bulb the usual route of invasion is through the tympanic floor; although 40% of recorded cases show intracranial spread, invasion of the jugular foramen is usually late. Two cases of glomus tumour are described. The first was initially diagnosed as a tumour of the cerebello-pontine angle. There were deafness, facial palsy, "black-outs", and occasional aphasic signs, with a dead labyrinth on the affected side. Craniotomy, after ligation of the external carotid artery, exposed a firm mass, 12×8 cm. in size, attached to the floor of the middle fossa and petrous ridge. The tumour was removed piecemeal and proved to be a glomus jugulare tumour; the patient, a man aged 67, made a good recovery. In this case, in spite of the unusual size of the intracranial mass, there was no damage to the jugular fossa nerves. In the second case, in a 40-year-old woman, there was a 5-year history of ear trouble, including removal of a polypus with considerable bleeding. The patient suffered from severe headache, a reeling gait, projectile vomiting, and loss of all function of the 6th to the 11th cranial nerves on the affected side, with slight sensory loss in the 5th nerve and some weakness in the 12th. There was also a systolic bruit over the mastoid. At operation a spherical tumour "the size of a lemon" was found which extended from the jugular foramen into the cerebello-pontine angle, compressing the brain stem. Attempts at removal resulted in severe haemorrhage. Later, the external carotid artery was ligated and most of the tumour removed, but the patient slowly deteriorated and died. The tumour was a glomus jugulare tumour.

In a third case described there were small skin lesions suggestive of neurofibromatosis (von Recklinghausen's disease). On the right side there was partial deafness of the middle-ear type, complete facial palsy, paralysis of the 9th, 10th, and 11th nerves, doubtful weakness of the 12th, and some loss of sensation on the right side of the face, with decreased corneal reflex. At operation a large tumour mass was found, apparently arising in the jugular fossa, growing around the internal carotid artery and spreading into the posterior fossa. The mass was removed; the patient made an uneventful recovery, but had some generalized headache and nausea which persisted. The tumour in this case was identified as a neurilemmoma. *F. W. Watkyn-Thomas*

998. **Cardiac Changes in Cranio-cerebral Trauma (Experimental Study).** (Изменения в сердце при черепно-мозговой травме (Экспериментальное исследование))
F. E. VISHNEVETSKII. *Вопросы Нейрохирургии* [*Vop. Nejrokhir.*] 30–34, No. 2, March–April, 1956. 4 figs., 19 refs.

Disturbances of cardiac function were observed in experimental animals in which closed cerebral injury was produced. These disturbances were reflected in the electrocardiogram and histologically were manifested as an alteration in the staining properties of the heart muscle and the presence of vascular stasis and haemorrhages. Additional functional loading was followed by the development of microscopic areas of cardiac infarction. *L. Crome*

999. **Capillaroscopic Observations in Cases of Trauma of the Cerebral Hemispheres.** (Капилляроскопические наблюдения при травмах больших полушарий головного мозга)
I. D. RIKHTER. *Вопросы Нейрохирургии* [*Vop. Nejrokhir.*] 34–39, No. 2, March–April, 1956.

The author describes the capillaroscopic changes observed in the skin in the course of 25 operations performed at Kursk Medical Institute for the extraction of foreign bodies from the brain; all the operations were carried out under local analgesia. During the injection of procaine there were transient spasms of the afferent arteries and temporary emptying of the capillaries. Handling of the dura was associated with blurring of the capillary network—the result of increased transcapillary exudation into the surrounding tissue. Similar blurring followed mechanical irritation of brain tissue, particularly in the parietal and occipital lobes. Manipulation of the deep layers of the brain was sometimes followed by changes in the character of the blood flow and in the degree of capillary filling. These last changes were particularly marked in operations on the temporal and occipital lobes. Irritation of the very deep layers and of subcortical formations resulted in retarded blood flow and prolonged stasis, which was most marked in operations on the temporal lobe. *L. Crome*

1000. **Sleep Treatment in Acute Cranio-cerebral Trauma.** (К вопросу лечения сном острой черепно-мозговой травмы)
L. Z. BERUCHASHVILI. *Вопросы Нейрохирургии* [*Vop. Nejrokhir.*] 49–51, No. 2, March–April, 1956.

The author reports, from Erevan, Armenia, the results of sleep treatment given to 60 patients suffering from recent acute brain injury. The early results were satisfactory in 50 of the cases. Long-term results, which could be assessed in 44 cases, compared favourably with those in 36 similar cases of trauma not treated by sleep therapy. The method used was administration of small doses of hypnotic drugs as soon as consciousness was

regained. These doses were increased on the 2nd and 3rd days, but towards the end of the treatment, which lasted for 4 to 10 days, were gradually decreased, sleep induced by means of conditioned reflexes being employed in the later stages of the treatment. *L. Crome*

1001. **Traumatic Cysts of the Brain.** (Über traumatische Hirncysten)
H. ROSENHAGEN. *Deutsche Zeitschrift für Nervenheilkunde* [*Dtsch. Z. Nervenheilk.*] **174**, 541–567, 1956. 8 figs., 9 refs.

Details are given of 7 patients admitted to the Provincial Hospital, Schleswig, who developed cysts of the brain following either open or closed head injuries. From a study of 5 of the cases which were under observation for over 4 years, with regular clinical and pneumoencephalographic examinations, a picture emerged which showed that these cysts act as slowly progressive lesions, increasing in size and causing progressive brain damage. This in turn leads to worsening of the clinical state and to increasing intellectual and personality deterioration of organic type. The possible patho-physiological changes underlying the formation and enlargement of the cysts are discussed in the light of the clinical, pneumoencephalographic, and operative findings, and the course and possible lines of treatment in such cases are indicated.
J. B. Stanton

1002. **The Surgical Treatment of Intracranial Aneurysms**
W. B. HAMBY. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Arch. Neurol. Psychiat.*] **75**, 345–349, April, 1956.

Out of a series of 163 verified cases of intracranial aneurysm admitted to the Buffalo General Hospital, the aneurysm was located by means of angiography in 69. Of these cases, 51 were treated surgically, with 11 deaths (a mortality of 21·5%) and 18 were untreated, also with 11 deaths (61%). Subarachnoid haemorrhage had occurred in 43 of the former and 15 of the latter cases. Of 7 patients operated upon within one week of the haemorrhage, 5 died, mortality becoming progressively less with longer intervals. The author discusses the merits of different surgical procedures, concluding in favour of direct occlusion of the aneurysmal neck wherever this is technically possible. *L. Crome*

1003. **Cerebral Hypoxia: Aetiology and Treatment**
D. E. ARGENT and D. H. P. COPE. *British Medical Journal* [*Brit. med. J.*] **1**, 593–598, March 17, 1956. 3 figs., 27 refs.

A number of papers have been published on cerebral hypoxia arising from a period of cardiac arrest. The present authors, from the Middlesex Hospital, emphasize that periods of hypoxia without cardiac arrest can start the vicious circle of anoxic damage to cerebral capillaries, increased permeability of those capillaries, cerebral oedema, impairment of oxygen transfer to cerebral tissue by the interposed oedema fluid, and more anoxia. The clinical picture, though variable, usually includes coma with stertorous respiration, hyperpyrexia, and athetoid limb movements. The aim of treatment is to relieve the oedema by intravenous administration of hypertonic solutions. The dehydrating substance used should not pass into the cerebrospinal fluid and should be excreted intact rather than metabolized, so that, like urea, it promotes a diuresis. The authors recommend 50% sucrose, but in view of some equivocal evidence that this causes renal damage, treatment is continued after the initial dehydration period is over with 10% dextran, especially if prolonged treatment is necessary. At first 40 ml. of the sucrose solution is given, followed by a further 60 ml. in the succeeding 40 minutes; thereafter, 10% dextran is administered by intravenous infusion at the rate of 50 ml. an hour. Adequate oxygenation through a perfect airway is essential, and a 7-degree head-down tilt promotes drainage of secretions without adding to the cerebral congestion.

The authors describe 3 cases in detail. They consider they are justified in advising dehydration therapy if there is only presumptive evidence of a cerebral hypoxic episode. *Donald V. Bateman*

1004. **Gastric Haemorrhage in Acute Intracranial Vascular Accidents**
A. DOIG and J. SHAFAR. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **25**, 1–19, Jan., 1956 [received April, 1956]. 10 figs., bibliography.

A clinical and pathological study of 7 cases in which gastric haemorrhage was a complication of acute intracranial vascular disease is reported from the Burnley Group of Hospitals, Lancashire. In 5 cases the intracranial lesions were due to cerebral haemorrhage, while in 2 subarachnoid haemorrhage was responsible. These 7 cases were observed within a period of 13 months, thus emphasizing the frequency of the condition. At necropsy in 5 cases the gastric lesions responsible for the haemorrhage were examined. Microscopically, there were multiple punctate haemorrhages in the stomach mucosa in all cases; in 2 cases small erosions were also present and in another small acute ulcers were noted. Using the Lepehne–Pickworth method with the benzidine stain, the authors were able to confirm previous observations that the haemorrhages were of venous origin.

The problem of the pathogenesis of these lesions is discussed, including the part played by the autonomic nervous system, since there is some evidence that stimulation of this system may lead to gastric erosion. The increase in excretion of corticosteroids following surgical operations and " many medical diseases " may also play a part by increasing the secretion of both acid and pepsin in the stomach. *Fergus R. Ferguson*

1005. **Acetazolamide in Treatment of Epilepsy**
B. ANSELL and E. CLARKE. *British Medical Journal* [*Brit. med. J.*] **1**, 650–654, March 24, 1956. 4 figs., 26 refs.

The authors report, from the Postgraduate Medical School of London, the effects of acidosis produced by the administration of acetazolamide (" diamox ") in the treatment of 26 patients with epilepsy. An initial dose of 125 mg. was given twice daily, this being progressively increased to 10 mg. per kg. body weight if necessary.

The drug was given alone in 15 cases and combined with standard anticonvulsants in the others. Side-effects were few and mostly transient, consisting of peripheral paraesthesiae, drowsiness, and depression, and treatment was continued for periods up to 20 months. The authors conclude from their results that acetazolamide is of some value as an anticonvulsant, either alone in major and minimal types of epilepsy, or as an adjuvant to other drugs in some cases of mixed type. The possible modes of action of the drugs are discussed. *J. B. Stanton*

1006. **Surgical Alleviation of Parkinsonism**
I. S. Cooper, N. Poloukhine, and A. Morello. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 1444–1447, April 28, 1956. 3 figs., 10 refs.

The results achieved in the treatment of far-advanced Parkinsonism by occlusion of the anterior choroidal artery (50 cases) and chemical destruction of the globus pallidus (50 cases) are reported in this paper from the New York University–Bellevue Medical Center. The anterior choroidal artery was occluded by electrocoagulation, the authors having previously found that silver clips alone were unreliable for this purpose. Experience showed that the postoperative complications of somnolence and pneumonia were much reduced if the operation was performed under local analgesia, supplemented, if necessary, with not more than 200 mg. of thiopentone. To lessen spasm of the internal carotid artery and its branches an infusion of papaverine hydrochloride or of dioxylene phosphate ("paveril") was given. Difficulties encountered included adhesion of the uncus to the arachnoid and oculomotor nerve palsy in some patients with post-encephalitic Parkinsonism. Good or excellent results were obtained in 30 patients, there being significant alleviation of both tremor and rigidity in the contralateral limb. In 12 cases the operation was unsuccessful, the reason in 5 being technical failure to obliterate the artery. There were 5 deaths and in 3 cases there was hemiplegia. Complications included oculomotor palsy (5 cases), which, however, cleared spontaneously, and quadrantic hemianopia (1 case). The authors rightly point out that the inherent disadvantage of this technique is the variability in the origin and distribution of the artery.

Chemical destruction of the globus pallidus (chemopallidectomy) was carried out as follows. After pneumoencephalography and under radiological control a trephine opening was made above the zygoma and a polyethylene cannula introduced so that its tip lay in the mesial globus pallidus. [This technique is described in detail.] Procaine was then injected, and if the situation was correct contralateral tremor was abolished. This was followed by slow injection of 0·4 ml. of alcohol over a period of 20 to 30 minutes. The wound was then closed with the cannula *in situ* so that two further injections of alcohol could be given during the ensuing week. Good and lasting results were obtained in 32 of the 50 cases. There were 2 deaths from serious complications; in addition, hemiplegia developed in one case and ataxia with oculomotor nerve palsy in another.

R. G. Rushworth

NEUROMUSCULAR DISEASES

1007. **Muscular Dystrophy. I. History, Clinical Status, Muscle Strength, and Biopsy Findings**
G. H. Fetterman, M. J. Wratney, J. S. Donaldson, and T. S. Danowski. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **91**, 326–338, April, 1956. 9 figs., 22 refs.

The authors, working at the University of Pittsburgh School of Medicine, have studied 31 cases (27 in males, 4 in females) of muscular dystrophy occurring in childhood. In about one-half of the cases there were other affected sibs, but only in one family had the disease occurred in earlier generations. The age of onset was between 2 and 10 years of age, and symptoms had been present for 6 months to 12 years when the patient was first seen. About 50% of the patients were no longer able to walk. The muscular strength of the limbs and trunk was assessed and graded according to an arbitrary scale in all cases, and the assessment was repeated after operation in those 22 cases which were subjected to muscle biopsy (usually from both the deltoid and gastrocnemius muscles). Loss of muscular power appeared to be greater in the legs than the arms; it appeared to affect all muscle groups symmetrically and was worse in the advanced cases, but there was no apparent deterioration after muscle biopsy. The characteristic histological appearances of muscular dystrophy as seen in biopsy specimens of muscle—namely, striking variation in fibre size, fibre splitting, and vacuolization and necrosis of the fibres, with phagocytosis—are described and illustrated; these changes too were more striking in the advanced cases.

[To anyone who has attempted to assess muscular power quantitatively the measurements recorded in this paper will not be acceptable. The figures given refer to the power of entire limbs and regions, no apparent attempt having been made to determine that of individual muscles, whereas selective weakness and atrophy of individual muscles is a well-recognized feature of muscular dystrophy. Thus to say, for instance, that the power of the lower limb was "38% of normal" is of no value for the assessment of the extent of the disease, besides being scientifically meaningless.]

John N. Walton

1008. **Muscular Dystrophy. II. Radiologic Findings in Relation to Severity of Disease**
B. Girdany and T. S. Danowski. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **91**, 339–345, April, 1956. 8 figs., 17 refs.

Radiographs were taken of the vertebral column, skull, long bones, wrist, and thorax of 31 children in whom the clinical picture and muscle biopsy findings indicated a diagnosis of progressive muscular dystrophy [see Abstract 1007]. Among the radiographic changes which were constantly observed in these cases were: scoliosis, lordosis, and an apparent increase in altitude of the vertebral bodies; coxa valga and subluxation of the hips; narrowing of the shafts of the long bones and

" modulation " or " overtubulation " of the metaphyses; osteoporosis; retardation of bone age; and increase in mass of the soft-tissue shadow of the calf muscles, with the subsequent development of " striation " indicating fatty infiltration. All of these changes were clearly related to the severity and duration of the disease, being more severe in the more advanced cases.

John N. Walton

1009. **Muscular Dystrophy. III. Serum and Blood Solutes and Other Laboratory Indices**
T. S. DANOWSKI, P. M. WIRTH, M. H. LEINBERGER, L. A. RANDALL, and J. H. PETERS. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **91**, 346–355, April, 1956. 9 figs., 36 refs.

The authors have carried out creatine tolerance tests, extensive haematological and metabolic studies, and a battery of hepatic and renal function tests on 31 children with muscular dystrophy [see Abstract 1007]. The well-recognized association of relative hypercreatinaemia and creatine intolerance with this disease was confirmed, but no significant haematological abnormality was discovered, nor was any consistent defect in renal or hepatic function demonstrated. However, it was found that serum calcium and phosphorus values in the patients with muscular dystrophy were somewhat higher than those obtained in normal control subjects of the same age, while cholesterol and chloride values were somewhat lower.

The authors discuss the possible reasons for these findings, but no definite conclusions are reached; it is possible that the high serum calcium and phosphorus levels may reflect a delay in biochemical maturation corresponding to that which occurs in physical development, or a decrease in the muscle mass which can participate in phosphorylation and glycolysis may be partly responsible. The subnormal serum cholesterol content may be the result of an unrecognized disorder of fat metabolism, the existence of which might explain the extensive fatty infiltration of the diseased muscles.

John N. Walton

1010. **Muscular Dystrophy. IV. Endocrine Studies**
T. S. DANOWSKI, R. M. BASTIANI, F. D. MCWILLIAMS, F. M. MATEER, and L. GREENMAN. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **91**, 356–364, April, 1956. 7 figs., 35 refs.

The authors have estimated the urinary output of pituitary gonadotrophins and 17-ketosteroids and carried out extensive tests of thyroid function and of carbohydrate metabolism on a group of 31 children with progressive muscular dystrophy [see Abstract 1007]. No abnormalities of gonadotrophin or 17-ketosteroid excretion were revealed. The serum protein-bound iodine level was often higher than in normal control subjects, but nevertheless the rate of disposal of a single dose of 0·2 mg. of thyroxine per kg. was normal, as judged from serial serum protein-bound iodine estimations in 6 cases; hence it is probable that in muscular dystrophy there is either increased production of thyroid hormone or an increase in the binding capacity of the serum proteins. Oral and intravenous glucose tolerance tests gave normal results, but the change in blood sugar level following the intravenous injection of insulin was less than normal; this reduction in insulin-induced glycolysis is presumably due to the diminution in the muscle mass or to its involvement in the disease.

John N. Walton

1011. **Muscular Dystrophy. V. Blood Sugar and Serum Electrolytes following Insulin and Dextrose, Alone or in Combination**
T. S. DANOWSKI, H. K. GILLESPIE, T. J. EGAN, F. M. MATEER, and M. H. LEINBERGER. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **91**, 429–435, May, 1956. 3 figs., 43 refs.

Continuing the series of studies of muscular dystrophy undertaken at the University of Pittsburgh School of Medicine, the authors have studied the effects of the intravenous injection of crystalline insulin, 0·1 unit per kg. body weight, and of dextrose, 0·5 g. per kg. as a 50% solution in water, given separately and in combination, on groups of children with the juvenile form of the disease varying in number between 10 and 23. Samples of venous blood were taken for blood sugar and serum electrolyte estimations before the injections and at half-hourly intervals afterwards, and the results were compared with those obtained in control groups of 10 to 27 normal children.

It was found that the changes in venous blood sugar level after insulin in the dystrophic subjects were similar to those in the control subjects, but the decreases in serum inorganic phosphorus, potassium, and bicarbonate levels which normally follow insulin administration were much less. The effects of dextrose alone were similar in the two groups but insulin and dextrose in combination consistently produced hyperglycaemia in the individuals with muscular dystrophy and hypoglycaemia in the control subjects. The authors conclude that the inadequate disposal of glucose which is evident in the dystrophic subjects is compatible with a decrease in extrahepatic utilization owing to widespread disease of the musculature.

John N. Walton

1012. **Muscular Dystrophy. VI. Diminished Blood Sugar and Serum Electrolyte Responses to Epinephrine**
E. B. FERGUS, W. R. NICHOLS, L. M. HORNE, and T. S. DANOWSKI. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **91**, 436–441, May, 1956. 4 figs., 21 refs.

The authors have studied the effects of adrenaline, given subcutaneously, on the blood sugar and serum electrolyte levels in patients with muscular dystrophy and in control subjects [see Abstract 1011]. The patients were fasting and 0·01 ml. of 1:1,000 adrenaline per kg. body weight was given divided in 3 doses at intervals of 10 minutes. Similar changes in pulse rate and blood pressure occurred in both groups. Samples of venous blood were obtained for blood sugar and serum electrolyte estimations before and 30, 60, 90, and 120 minutes after the injection.

The hyperglycaemic response was consistently less in the cases of muscular dystrophy than in the control

subjects, as was the fall in serum inorganic phosphorus and serum potassium levels. These findings may reflect a diminished activation of liver phosphorylase by adrenaline, a lack of response of the hepatic glycogen stores to phosphorylase, or depletion of the liver glycogen stores in the individuals with muscular dystrophy. An alternative explanation, in conflict with current views, is that adrenaline hyperglycaemia results partly from a release of liver glycogen and partly from a conversion of muscle glycogen and that the diminished hyperglycaemic response in dystrophic individuals is due to the low glycogen content of the diseased muscles. In addition to these possibilities a decreased contribution from gluconeogenesis cannot be excluded.

[Unfortunately the authors do not give clear information concerning the age and clinical condition of the patients or the number of cases investigated.]

John N. Walton

1013. **Muscular Dystrophy. VII. Trials of a Pituitary Growth Factor**

T. S. DANOWSKI, L. GREENMAN, F. M. MATEER, M. J. WRATNEY, and J. S. DONALDSON. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **91**, 442–448, May, 1956. 3 figs., bibliography.

In view of the effect of pituitary growth hormone in increasing the size of muscles and organs in experimental animals, with retention of nitrogen and electrolytes, 4 children between 4 and 7 years of age with muscular dystrophy were given intramuscular injections of a "non-diabetogenic" preparation of the hormone for 6 to 8 months in a daily dosage of 3 mg. per kg. body weight. The material was prepared in accordance with the procedure of Raben and Westermeyer (*Proc. Soc. exp. Biol. (N.Y.)*, 1952, **80**, 83; *Abstracts of World Medicine*, 1952, **12**, 541) and was shown to restore growth in hypophysectomized mice. During the course of treatment detailed studies of muscular strength were made and repeated haematological, biochemical, and endocrinological investigations were performed.

The preparation had no apparent toxic effects, but it failed to influence the course of the muscular disease. Insulin tolerance and glucose tolerance were not affected, and there was no evidence of stimulation of the thyroid gland, adrenal cortex, or gonads. The fact that all 4 patients developed crops of freckles soon after treatment was begun suggests that the preparation contained a melanophore factor. *John N. Walton*

1014. **Muscular Dystrophy. VIII. Trials of Protein Hydrolysate, Vitamin Supplements, and Physical Therapy**

J. S. DONALDSON, M. J. WRATNEY, A. PASCASSIO, F. A. WEIGAND, and T. S. DANOWSKI. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **91**, 449–453, May, 1956. 10 refs.

A series of 29 children between 2 and 15 years of age who were suffering from muscular dystrophy was divided into 3 groups. One of these received no treatment apart from vitamin supplements; another group were given the regimen of protein hydrolysate and vitamins which Van Meter has claimed to be effective (*Calif. Med.*, 1953, **79**, 297), while the third group was treated with protein hydrolysate and vitamins together with physical therapy in the form of frequent graded exercises. Treatment was given over a prolonged period [though the exact duration is not stated] and repeated measurements of muscular strength and estimations of the blood sugar, cholesterol, and electrolyte levels were made. The results were compared with those obtained with physical therapy alone and with no special treatment.

The disease continued to progress in all cases, though in some instances there was an apparent temporary improvement; this, however, could invariably be attributed to the acquisition of new skills as a result of training. The authors were not able to determine whether any of the regimens tested was effective in slowing the rate of deterioration. Protein-hydrolysate therapy did not appreciably alter the moderate elevation of serum calcium and phosphorus levels which the authors have previously demonstrated in cases of muscular dystrophy.

John N. Walton

1015. **Amyotonia Congenita. A Follow-up Study**

J. N. WALTON. *Lancet* [*Lancet*] **1**, 1023–1028, June 30, 1956. 28 refs.

The author has determined, by correspondence or personal examination, the eventual outcome of 109 out of a total of 115 cases collected from the records of a number of hospitals in which the diagnosis of amyotonia congenita had been made in infancy 2 to 25 years earlier. Revision of the diagnosis in the light of subsequent developments showed that 67 of the patients were suffering from the infantile spinal muscular atrophy of Werdnig and Hoffmann; of this group, 55 had died, invariably of respiratory infection, the majority dying between the ages of 3 months and 4 years; the 12 survivors were all severely disabled by muscular atrophy and contractures. A further 17 patients fell into a group called by the author "benign congenital hypoplasia"; 8 of these had recovered completely and 9 showed some improvement but remained moderately disabled; the cases in this group closely resembled those described by other authors as "congenital myopathy" and as "congenital universal muscular hypoplasia". The remaining cases were examples of other neuromuscular disorders, such as progressive muscular dystrophy starting in infancy (3 cases) and polymyositis (1 case), or of unrelated conditions such as cerebral palsy (6 cases) and scurvy (twin sisters).

[This is a most careful and valuable study, comparable with the follow-up of similar cases carried out in Denmark by Brandt in 1950. It confirms the suggestion made by Batten that amyotonia congenita is a syndrome caused by various pathological processes rather than a distinct disease.] *J. W. Aldren Turner*

1015(*a*). **Familial Peroneal Muscular Atrophy and its Association with the Familial Ataxias and Tremor and Longevity**

R. HIERONS. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **19**, 155–160, May, 1956. 19 refs.

Psychiatry

1016. **Parkinsonian Reactions following Chlorpromazine and Reserpine. Similar Reactions in the Same Patients**
R. H. MAY and G. E. VOEGELE. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Arch. Neurol. Psychiat.*] **75**, 522–524, May, 1956. 10 refs.

Four cases are reported in which a Parkinsonian syndrome developed during chlorpromazine administration and also under reserpine medication, each drug given singly. The hypothesis is offered that one or more identical areas in the central nervous system are affected by direct or referred action of either drug.—[Authors' summary.]

1017. **Psychological Disturbances in Cerebro-hypophysial Cachexia.** (К вопросу о психических расстройствах при церебрально-гипофизарной кахексии)
M. G. MALKINA and A. V. ARKHANGEL'SKIĬ. *Проблемы Эндокринологии и Гормонотерапии* [*Probl. Endokr. Gormonoter.*] **2**, 3–7, No. 1, Jan.–Feb., 1956. 2 figs., 20 refs.

The authors describe the case of a young man of 20 with congenital syphilis who developed diabetes insipidus after tonsillectomy and in whom, a year later, mental changes (such as negativism, antagonism to relatives, delusions of poisoning, temporary hallucinations, apathy and irritability) suggestive of schizophrenia appeared. The face, axillae, and pubis were devoid of hair, severe normochromic anaemia was present, and the blood sugar level was 67 mg. per 100 ml. [but it is not stated whether this was taken fasting or not]. In examination of the cerebrospinal fluid for globulin, the Pandy, Nonne-Apelt, and Weichbrodt tests all gave strongly positive results. The Wassermann reaction was negative, although at the age of 10 it had been positive. Radiological examination of the lungs and sella turcica showed no deviation from normal.

The patient was treated with penicillin, " adiurekrin ", and the intravenous administration of glucose and vitamins; after 2 months there was some improvement in the general and mental condition, but later he became blind from primary optic atrophy, developed a subfebrile temperature, and died about a year after the onset of mental symptoms.

Necropsy revealed syphilitic arteritis and diffuse gummatous infiltration extending throughout the midbrain and the optic chiasma. The pituitary gland was not so affected, but the anterior lobe showed a predominance of basophil cells and the pars intermedia numerous colloid areas; no changes were apparent in the posterior lobe. Pigmentation with lipofuchsin, dystrophy, and cell necrosis was found in the cerebellar ganglia, pons, and the walls of the third ventricle. The thyroid gland and testicles were sclerosed and atrophied, and the capsules of the adrenal glands were thickened. The vessels of the thymus were full of blood and the number of Hassall's corpuscles was diminished; most of the cells were lymphocytes.

An extensive review of the literature [mainly Russian] showed that similar changes have been observed in Cushing's syndrome, tumours of the midbrain, diencephalic cachexia, Simmonds's disease, and other hypophysial–midbrain disturbances. Regarding the subfebrile temperature, the majority of authors report hypothermia in this type of cachexia. Shapiro and Itsenko, however, regard a continuous subfebrile temperature as an indirect result of disturbance of thermoregulation, as is also the " chilliness " so often observed in these patients. *L. Firman-Edwards*

1018. **Addiction to Methylated Spirit**
A. A. MACDOUGALL and K. MACAULAY. *Lancet* [*Lancet*] **1**, 498–500, April 21, 1956. 2 refs.

An account is given of 60 cases of addiction to methylated spirit admitted to Gartloch Hospital, Glasgow, between March, 1950, and July, 1955. Only one of the addicts was a woman. All the patients originally drank the commoner beverages, and turned to methylated spirit and its compounds (boot polish, brass polish, shellac, and paints) for economy. They all showed group characteristics of emotional blunting, a tendency to vagrancy, pessimism, and depression, but were not actively psychotic, and responded to therapy at least as well as other addicts, sometimes better. Treatment consisted in detoxication and sedation followed by the administration of vitamin-B complex with vitamin C and potassium bromide, 4 g. twice a day. The latter was given to replace loss of sodium chloride as well as for its sedative action, depletion of sodium chloride from tissue fluids being considered the chief cause of craving. This was augmented by psychotherapy and group therapy, the latter being provided by Alcoholics Anonymous. Disulfiram as a remedy was considered unsafe because of the possibility of the release of formic acid by its chemical reaction with methyl alcohol.

The authors' most striking conclusion is that, contrary to popular opinion, methylated-spirit drinking is not " the last stage of alcoholic excess ", and, the chief cause being poverty, the prognosis is at least as good as with other addicts. *R. J. Matthews*

1019. **Anxiety States**
G. GARMANY. *British Medical Journal* [*Brit. med. J.*] **1**, 943–946, April 28, 1956. 3 refs.

Among 644 patients who attended the psychiatric outpatient clinic of Westminster Hospital, London, 158 (25%) suffered from anxiety states. Constitutional and personality factors were found to be more important aetiologically than such external factors as housing or marital and domestic difficulties. The incidence of anxiety states was highest in the fourth decade, 66 (40%)

of the patients being in the age group 31–40. Treatment consisted in the administration of sedatives, in psychotherapy which was mainly supportive and re-educative, and in relaxation exercises. *F. K. Taylor*

1020. **Reserpine in Anxiety States**
E. H. HARE, C. P. SEAGER, and A. LEITCH. *Lancet* [*Lancet*] **1**, 545–547, April 28, 1956. 9 refs.

A comparative investigation of the effects of reserpine, amylobarbitone sodium, and an inert substance in 33 patients suffering from neurotic anxiety is reported in this paper from Barrow Hospital, Bristol. The dosage of reserpine was 2 mg. three times a day and that of amylobarbitone 2 gr. (0·13 g.) three times a day, the two drugs and the placebo being each administered for one week.

A self-controlled, self-recorded technique of assessment was used, the reliability of the patients' records being checked against those kept by a nurse and the physician in charge. Most of the patients recorded significant alleviation of anxiety symptoms while they were receiving amylobarbitone sodium, but no general tendency to alleviation during reserpine therapy.
J. MacD. Holmes

1021. **Benactyzine in Psychoneurosis, with a Note on the E.E.G. Changes in Normal Subjects**
M. J. RAYMOND and C. J. LUCAS. *British Medical Journal* [*Brit. med. J.*] **1**, 952–954, April 28, 1956. 9 refs.

Benactyzine ("suavitil") is the hydrochloride of benzilic acid diethylaminoethyl ester. In a small trial at St. George's Hospital, London, out of 18 patients with anxiety neurosis, 12 were "improved" or "considerably improved". However, patients with obsessional, hysterical, or depressive symptoms did not respond well. Side-effects were frequent, the chief complaint being a feeling of heaviness in the limbs. In electroencephalographic studies carried out at University College Hospital, London, the tracing showed a marked diminution in the amount of alpha rhythm in 5 out of 10 normal subjects given the drug by intravenous injection.
F. K. Taylor

1022. **"Meratran". A New Stimulant Drug**
W. G. A. BEGG and A. A. REID. *British Medical Journal* [*Brit. med. J.*] **1**, 946–949, April 28, 1956. 7 refs.

In a clinical trial carried out at St. Thomas's Hospital, London, on over 200 psychiatric patients and 24 normal subjects, "meratran" (alpha-(2-piperidyl) benzhydrol hydrochloride) was found to produce an elevation of mood, not amounting to euphoria, in the normal person, and did not adversely affect appetite or sleep. In patients with reactive depression but without symptoms of anxiety, hysteria, or obsession, good therapeutic results were obtained with a dosage up to a maximum of 7·5 mg. per day given divided in three doses. In cases of endogenous depression the results were not so good, and some patients became worse. In the treatment of spasmodic torticollis some improvement was achieved with high doses (up to 35 mg. a day) in 4 out of 5 cases, but only one patient was completely relieved. The lethargy occurring after leucotomy in some patients seemed to respond well. However, as the authors point out, the danger of causing psychotic reactions, even with small doses of the drug, reduces its value in general practice and in out-patient clinics. *F. K. Taylor*

1023. **A Clinical Study of Miltown, a New Tranquilizing Agent**
L. S. SELLING. *Journal of Clinical and Experimental Psychopathology and Quarterly Review of Psychiatry and Neurology* [*J. clin. exp. Psychopath.*] **17**, 7–14, Jan.–March, 1956. 7 refs.

The effect of meprobamate (2-methyl-2-*n*-propyl-1:3-propanediol dicarbamate; "miltown"), an interneuronal blocking agent, in the treatment of 200 psychiatric cases seen in private practice is described. The usual dosage was 1,600 mg. a day and the duration of treatment ranged from 4 weeks to 8 months. Withdrawal was gradual, and in most cases was begun after 3 months' treatment. There was improvement or recovery in 90% of the patients with anxiety, 60% of those with conversion hysteria, and 90% of the alcoholics. Major psychoses were much less responsive, particularly psychotic depression, although hypomania was sometimes controlled. Symptoms of tension, tension headache, and non-psychotic insomnia improved, and patients became more responsive to psychotherapy. Side-effects, which were not frequent, included gastric discomfort and allergy. Toxicity appeared to be slight; as much as 40 g. of the drug in one day, which the patient had hoarded, produced only deep somnolence. It is concluded that meprobamate is an effective and safe tranquillizer which does not give rise to addiction. *A. C. Tait*

1024. **A Controlled Study of Chlorpromazine Therapy in Chronic Psychotic Patients**
S. S. TENENBLATT and A. SPAGNO. *Journal of Clinical and Experimental Psychopathology and Quarterly Review of Psychiatry and Neurology* [*J. clin. exp. Psychopath.*] **17**, 81–92, Jan.–March, 1956. 11 refs.

From Saint Elizabeth's Hospital, Washington, D.C., a clinical trial of chlorpromazine in the treatment of disturbed psychotics is reported, the patients being 50 female negroes aged 8 to 57 years; 50 similar patients served as controls. The duration of illness ranged from one year to 24 years. The patients were given an intramuscular injection of 50 mg. of chlorpromazine on the first day of treatment, 100 mg. on the second, and 150 mg. on the third; thereafter they received the drug by mouth in a daily dosage of 300 to 900 mg. The duration of treatment was deliberately varied from 16 to 116 days. A response to the drug was usually evident at 20 days; if, however, there was no response after 50 days none could be expected. The condition remained unchanged in only 20% of the patients given chlorpromazine compared with 90% of the controls. The age of the patient, duration of the illness, and previous therapy did not influence the results, but manic, catatonic, and paranoid types responded best. Toxic effects were frequent but not severe; the commonest complication [oddly] was lactation, which occurred in 18 of the 50 patients, usually about the eleventh day. *A. C. Tait*

Dermatology

1025. **The Pathogenesis of Milia and Benign Tumors of the Skin**
W. EPSTEIN and A. M. KLIGMAN. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **26**, 1–11, Jan., 1956. 4 figs., 17 refs.

By definition milia are small retention cysts of sweat-gland ducts. The authors, in this paper from the University of Pennsylvania, Philadelphia, use the term milia for all small keratin-filled cysts seen in the skin, and proceed to demonstrate that the majority of such structures are not of sweat-gland origin. They have studied clinical milia occurring on otherwise normal skin of the face and the similar lesions seen in epidermolysis bullosa, after dermabrasion, and in autografts. The majority of cysts of the type described arise from hair follicles in the region of the sebaceous glands. They are especially frequent in the sebaceous-gland rudiments curiously shaped like an inverted cup which often surround downy hairs (the *mantelhaare* of Pinkus). Identical structures can be traced, however, arising from epidermis or sweat glands. The significance of this as evidence of the pluripotentiality of epithelial cells is discussed, particularly in relation to the histogenesis of skin tumours. The authors regard milia as tumours. [The possible relation to sebaceous cysts is not discussed.]

Bernard Lennox

1026. **Primary Skin Cancer of the Fingers Simulating Chronic Infection**
H. T. JOHN. *Lancet* [*Lancet*] **1**, 662–664, May 12, 1956. 1 fig., 9 refs.

From University College Hospital, London, the author reports 5 cases of primary skin cancer of the fingers simulating chronic infection. In 3 cases a squamous-celled carcinoma was present, the sites being, respectively, the distal phalanx of the thumb, the radial side of the proximal phalanx of the index finger, and the dorsum of the first web. In each of the 2 remaining cases there was a malignant melanoma under the thumb nail. Inflammatory lesions had been diagnosed in 3 cases. The difficulties of clinical diagnosis are emphasized; it is suggested that biopsy should be performed in all cases in which an ulcerated lesion of the fingers is slow to heal and there is no obvious cause for chronicity.

Bernard Lennox

1027. **Long-term Management of Pemphigus Vulgaris with Corticotropin (ACTH)**
R. B. STOUGHTON. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 1011–1014, March 24, 1956. 3 figs., 6 refs.

The successful management of 9 cases of definite pemphigus vulgaris by administration of ACTH is reported from the University of Chicago. Treatment was given for 1½ to 4½ years, during which time all the patients experienced periods of remission when ACTH was not needed, and periods of exacerbation when greatly increased doses and, in some cases, admission to hospital were necessary. Side-effects were minimal and control of blister formation was excellent. Five of the cases are described in detail. The author concludes that adequate control of pemphigus vulgaris with ACTH for indefinite periods of time is " entirely possible ".

G. B. Mitchell-Heggs

1028. **A Note on the Natural History of Lichen Planus**
P. D. SAMMAN. *British Journal of Dermatology* [*Brit. J. Derm.*] **68**, 175–181, May, 1956. 3 figs., 3 refs

As a contribution to the natural history of lichen planus the author reports that of 121 cases of the disease seen at Westminster Hospital, London, 38 were treated with acetarsol, 1 gr. (65 mg.) daily by mouth, 39 with 0·1% solution of perchloride of mercury, 3·5 ml. 3 times a day by mouth, and 44 patients, who served as controls, were given a bland substitute for these drugs. All the patients had typical acute and subacute papules.

In the time taken for the eruption to clear after the treatment began there was no significant difference between the three groups. The progress of the condition was investigated in 102 patients, 32, 33, and 37 respectively from the three groups. Of these patients, both treated and untreated, 23% were clear of skin lesions after 6 months, 64% after one year, 85% after 18 months, and 97% after 2 years. Over one-fifth of the patients had more than one attack of lichen planus and the age at onset varied between 20 and 82 years. In 77% the buccal mucosa was affected and there was evidence of this after the skin lesions had faded. Deformities of the nails were seen in 11 patients, but none had alopecia. The author found [contrary to the experience of many other dermatologists] that emotional factors were of importance in only a minority of the patients.

S. T. Anning

1029. **Psoriasis and Cerebral Lesions.** (Psoriasis und pathologische cerebrale Veränderungen)
B. STREITMANN. *Zeitschrift für Haut- und Geschlechtskrankheiten* [*Z. Haut- u. GeschlKr.*] **20**, 273–278, May 15, 1956. 13 refs.

The author describes from the Home for the Aged, Klosterneuburg, Vienna, the cases of 3 elderly patients who suffered from psoriasis which had resisted all treatment for 10 months to 2 years and who sustained cerebral lesions (minor stroke, an acute cerebral arteriosclerotic episode, and cerebral oedema respectively). In each of these patients there was a striking improvement of the skin lesions within a day or two of the onset of the cerebral symptoms. In 2 cases the psoriasis returned within 6 weeks, but the third patient was still clear 10 months later. The possibility of a causal relationship between cerebral lesions and the course of psoriasis is discussed.

G. W. Csonka

Paediatrics

1030. **Growth of the Skull in Young Children. I. Standards of Head Circumference. II. Changes in Head Shape**
C. K. WESTROPP, C. R. BARBER, and D. HEWITT. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **19**, 52–56, Feb., 1956. 4 figs., 17 refs.

Enlargement of the head in adults can only result from a gross pathological lesion, but in children it may be due to natural growth. It is important therefore to establish normal increments for each phase of the growing period. Serial measurements were made of the heads of 331 boys and 333 girls included in the Oxford Child Health Survey five times during their first year and at 6-monthly intervals up to the age of 5 years, and in 400 cases also at the age of 7. The circumference round the supraorbital margins and the most prominent part of the occiput was measured. The mean values for boys were slightly greater at all ages, the difference diminishing with age. Growth curves showed progression to be remarkably even throughout the period, and it is suggested that the " normal " values found in standard textbooks, which produce an uneven curve, have not been derived from serial measurements on the same children.

In the second part of the paper growth in the transverse and longitudinal diameters of the head in the same series is compared with the over-all increase in circumference. Both sexes were more brachycephalic at the age of 7 than at birth, the boys to a lesser extent than the girls. In both the cephalic index (ratio of breadth to length) increased rapidly during the first 6 months to reach a maximum at 9 months. Thereafter the index declined fairly rapidly in boys and at 5 years had almost regained its original level. In girls, however, the index declined more slowly and by the age of 3 years the relatively brachycephalic skull characteristic of the female had become evident. These findings are similar to those of two other reported series, one of American and the other of Scottish children. In all the mean skull diameter was greater in boys and the mean cephalic index was greater in girls, reaching a peak value before 12 months. Compared with the two British series, however, the American children had smaller, more brachycephalic heads. *J. G. Jamieson*

1031. **Observations on Dysostosis Enchondralis in Children.** (Zur Dysostosis enchondralis im Säuglingsalter)
N. URBAN. *Archiv für Kinderheilkunde* [*Arch. Kinderheilk.*] **153**, 238–251, 1956. 12 figs., 36 refs.

1032. **Factors Influencing Duration of Breast Feeding**
E. B. JACKSON. *Pediatrics* [*Pediatrics*] **17**, 700–715, May, 1956. 1 fig., 31 refs.

NEONATAL DISORDERS AND PREMATURITY

1033. **Control of Staphylococcal Infection of the Newborn by the Treatment of Nasal Carriers in the Staff**
P. M. ROUNTREE, M. HESELTINE, J. RHEUBEN, and R. P. SHEARMAN. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 528–532, March 31, 1956. 1 fig., 5 refs.

The investigation described herein was prompted by the increasing incidence of staphylococcal infection among newborn infants at King George V Hospital, Sydney, which was first apparent in August, 1953, and became pronounced in February, 1955. While previous investigations had shown that nasal carriers among nursing staff were the source of such infections, the wearing of masks by the staff as well as by all who came into contact with the newborn infant had not been successful in reducing the spread. It was therefore decided to try the effect of " neotracin " ointment applied to the nasal mucosa of carriers of *Staphylococcus aureus*. Since this ointment contains two antibiotics not used for parenteral or oral therapy—namely bacitracin and neomycin—it was unlikely that organisms insensitive to these drugs would be encountered. For various reasons only nursing staff were treated, roughly half of whom were found to be carriers. The ointment was applied to the nasal mucosa 3 times a day for one week; swabs were examined a week after treatment finished and again a month later. When the second swab was taken it was found that 35% of the nurses had ceased to be carriers. The authors state that half the failures were due to inadequate application, and that although the control of carriers was not perfect, there was a prompt and sustained reduction in the neonatal infection rate, probably by a " reduction in the over-all load of staphylococci " in the nurseries. *Margaret D. Baber*

1034. **Blood Pressure in the Newborn Estimated by the Flush Method**
J. O. FORFAR and M. A. KIBEL. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 126–130, April, 1956. 4 figs., 11 refs.

The authors report, from the University of Edinburgh, the results of the estimation of the blood pressure in 143 mature newborn infants by the " flush " method first proposed by Gaertner more than 50 years ago. In all, 513 estimations were carried out during the first 11 days of life; the method used was a modification of that described by Goldring and Wohltmann (*J. Pediat.*, 1952, **40**, 285). The results showed that the blood pressure increased significantly with age, and was not related to the sex of the infant. A comparison of the blood pressure in three groups of infants of birth weight 5 to 7, 7 to 8, and 8 to 11 lb. (2·2 to 3, 3 to 3·5, and 3·5 to 5 kg.) respectively, showed that there was a significant rise with

increasing birth weight. Estimations were usually made in pairs, on the arm and leg simultaneously in each infant; in 90% of cases the reading was higher in the leg than in the arm, a finding which, as the authors point out, should be useful in the diagnosis of coarctation of the aorta. The effect of crying was also studied in 67 infants paired for age and weight with an equal number of non-crying infants; crying caused an increase in blood pressure of less than 10% in the arm and less than 7% in the leg.

[This study has established the normal range of blood pressure during the first 11 days of life in mature infants and should serve a very useful purpose.]

David Morris

1035. **Erythroblastosis Fetalis. Pathologic Report on the Hearing Organs of a Newborn Infant**

G. KELEMEN. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **63**, 392–398, April, 1956. 6 figs., 26 refs.

Haemolytic disease of the new-born or of the foetus does not always cause the pigmentation of basal ganglia described as kernicterus; on the other hand, although kernicterus is usually associated with Rh incompatibility, it may occur independently, for example, in prematurity. Damage to the cochlear nuclei had been noted by many authors, but the first clinical proof of deafness due to kernicterus was advanced by Coquet in 1944. It was then shown by Goodhill that the incidence of haemolytic disease of the newborn was higher among nerve-deaf children than in the general population. In kernicterus this is due to damage to the nuclear centres, but in many of these cases there is no sign of central damage, and it must be assumed that the lesion is peripheral; on this point, however, the evidence is scanty. Only in 3 cases has histological examination been carried out. In 2 fatal cases of kernicterus in the neonatal period reported by Garrard there was sufficient damage to the cochlear nuclei in each case to cause total deafness had the child survived, but in neither was there any abnormality of the end organ.

The present author describes a third case in a 2-day-old child who was admitted to hospital with jaundice and found to have a Type-A Rh-positive reaction; the child died a few hours later. At necropsy there was no evidence of kernicterus in the brain. In the ears the otic capsule was well developed, with rare interruption of the endosteal layer; otherwise the only abnormalities were in the membranous labyrinth. The vestibular end-organs and organ of Corti were normal but the membrane of Reissner on both sides was depressed from the basal turn to the helicotrema and was in contact with the tectorial membrane; on both sides also the saccus endolymphaticus was dilated, but the tissue of the rugae was not compressed, but rather loosened by oedema. Oedema is " the only common denominator " in the findings, and oedema, followed by icterus, is the first sign of the disease. The present author inclines to Kristensen's view and does not fully believe that it is possible " to read the intravital pressure of labyrinthine fluid systems in the histological picture ". He discusses the use of the term " congenital " deafness in these cases. Strictly speaking deafness develops during early life, and may remain as the only sign of the disease; but here again it is difficult to distinguish between the Rh factor and some non-specific factor acting at the same time. He suggests that probably not more than 0·01% of " congenital " deafness is the result of Rh incompatibility. An interesting technical point is the possibility that the cells of Corti are to some extent preserved by congealing of the exudate between death and fixation. *F. W. Watkyn-Thomas*

1036. **A Study of Serum Bilirubin Levels in Relation to Kernikterus and Prematurity**

T. C. MEYER. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 75–80, April, 1956. 7 figs., 25 refs.

Kernicterus of prematurity, independent of any blood-group incompatibility, is now a well-recognized syndrome, but little is known of the serum bilirubin level in such cases and its relation to that found in full-term and healthy premature babies. The author therefore determined the bilirubin content of the blood and in some cases of the cerebrospinal fluid (C.S.F.) of 192 babies of all weight groups born at Sorrento Maternity Hospital, Birmingham, on one or more occasions during the first week of life; 11 of these infants developed kernicterus without evidence of blood-group incompatibility. The level of bilirubin in the blood in those developing kernicterus was similar to that in full-term infants with haemolytic disease, that is, more than 18 mg. per 100 ml.; there was no correlation between the serum and C.S.F. levels of bilirubin.

It is suggested [wisely] that serial serum bilirubin estimations should be carried out on all jaundiced premature infants and that exchange transfusion should be undertaken in those with rapidly rising levels to ensure that the critical level is not reached. In very small infants (under 4 lb. 6 oz. (2,000 g.)) the estimations will need to be repeated until the 6th or 7th day, when the peak level is reached. In full-term infants the peak occurs within 4 days. *Wilfrid Gaisford*

1037. **Incidence of Retrolental Fibroplasia: Past and Present**

T. M. SHAPIRA, S. M. SCHALL, H. FEINHANDLER, and D. KANE. *Journal of Pediatrics* [*J. Pediat.*] **48**, 640–646, May, 1956. 1 fig., 8 refs.

In the first part of this paper from the Michael Reese Hospital, Chicago, a retrospective survey is reported of 445 premature infants born between 1922 and 1951 who weighed 1,250 g. or less at birth and who survived until discharge from the Premature Unit. All were nursed in incubators in an atmospheric concentration of approximately 35 to 40% of oxygen. At the time of the survey 30 of the patients could not be traced. Of the remaining 415, 22 (5·3%) became blind (including 5 who were blind in one eye only) as a result of retrolental fibroplasia.

The second part describes an investigation carried out over a recent 2-year period in which 432 infants who weighed 2,140 g. or less at birth were subjected to ophthalmoscopic examination once during the first 3 weeks of life and then weekly until discharge, and were

followed up until they reached one year of age. Altogether, 35 (8%) showed signs of retrolental fibroplasia in varying degrees, which regressed in 24 and progressed to an advanced stage in 11 cases. The incidence of blindness among those under 1,500 g. at birth was 5% and among those between 1,500 and 2,140 g. less than 1%.

John Lorber

1038. **The Rise and Fall of Retrolental Fibroplasia in New York State. Preliminary Report**

A. YANKAUER, H. JACOBZINER, and D. M. SCHNEIDER. *New York State Journal of Medicine* [*N.Y. St. J. Med.*] **56**, 1474–1477, May 1, 1956. 1 fig., 6 refs.

Statistical evidence is presented of the dramatic fall in the incidence of retrolental fibroplasia in New York State following recognition of the part played by oxygen in the aetiology of the condition and the rigid control of the concentration of oxygen (to less than 40%) delivered to premature infants. The incidence of the disease reached a peak in 1953, but has been falling steeply since 1954. The number of infants classified as blind during the first year of life increased from 4 in 1946 to 52 in 1953 and fell to 3 in 1955. Of 69 certified blind infants followed up in 1955, all except one had been exposed to high concentrations of oxygen for prolonged periods. It is emphasized that continued vigilance by all concerned with premature infants is essential for the control of the disease.

C. A. Brown

1039. **Hyaline Membrane Disease: Its Nature and Etiology**

M. J. G. LYNCH, L. D. MELLOR, and A. R. BADGERY. *Journal of Pediatrics* [*J. Pediat.*] **48**, 602–632, May, 1956. 29 figs., 35 refs.

In previous investigations the authors have shown that the membranes lining the alveoli in hyaline membrane disease of premature infants contains an iron–porphyrin compound which can be identified microspectroscopically as a haemoglobin. It was also found that animals exposed continuously to a high oxygen tension became ill long before structural changes became evident in their lungs and that the development of acidosis and ketonuria preceded oedema and membrane formation in the lungs, which was a terminal phenomenon. They now report further experiments carried out at the General Hospital, Sudbury, Ontario, which were designed to define the nature, extent, and aetiology of the metabolic changes which apparently lead to the formation of hyaline membrane in the lungs of animals exposed to high oxygen tensions. White rats, guinea-pigs, and rabbits were used, and were placed in glass jars or wooden boxes supplied with an oxygen flow of 3 to 7 litres per minute. [The concentration of oxygen attained is not stated.]

Rabbits exposed to high oxygen tension showed a severe fall in the *p*H of the blood and a considerable rise in the serum potassium and inorganic phosphate levels, but only a slight fall in the carbon dioxide combining power of the blood. There was an increase in erythrocyte fragility, and urinary potassium excretion tended to be high. Similar results were obtained in rabbits and guinea-pigs subjected to bilateral vagotomy but not exposed to oxygen. The electrocardiogram in both groups of animals showed gross changes in the QRS complex, often with arrhythmia, signs of left heart strain, and other abnormalities, but these were of different types.

The animals exposed to oxygen developed severe and sudden heart failure in the terminal stages, and in view of the atypical electrocardiographic changes the authors consider that this failure may be due not to a high concentration of potassium in the tissue fluids, but rather to a low concentration of potassium in the cardiac muscle. [No figures are given to support this theory.] They suggest that this type of cardiac failure, which has hitherto not been appreciated, may be the underlying causative factor in hyaline membrane disease. It is also suggested that the dramatic biochemical upset which follows bilateral vagotomy, and which has not been previously noted, points to a basic vagosympathetic control of electrolyte and acid–base balance. These theories are discussed at length, and it is concluded that the naturally occurring and the experimentally produced diseases are of common aetiology, being due to the toxic effects of oxygen, the initiating factor being abolition of the afferent vagal chemoreceptor impulses from the lungs which results in unrestrained sympathetic action and a condition of secondary shock.

[There would appear to be a large difference between the highly artificial conditions to which the animals studied by the authors were exposed and those which give rise to hyaline membrane disease in premature infants. The suggestion that oxygen poisoning is responsible for the latter, though interesting, is therefore far from proven. The authors' lengthy discussion, extending over 15 pages, cannot be adequately summarized, and for details of this the original should be consulted.]

John Lorber

1040. **Radiological Findings in the Lungs of Premature Infants**

J. FAWCITT. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 119–123, April, 1956. 3 figs., 4 refs.

The value of chest radiographs in the clinical management of respiratory difficulties in premature infants is discussed in this paper from Crumpsall Hospital, Manchester. The author, using a standard mobile apparatus kept permanently in the premature infants' ward, subjects each infant on admission to *x*-ray examination of the chest. During a recent 18-month period 190 premature infants were so examined; in 25 of 141 infants who survived there was clinical respiratory distress and the radiographs revealed pathological changes in the lungs. The conditions observed could be divided into the following broad categories: (*a*) prematurity or immaturity, leading to complete or almost complete primary atelectasis; (*b*) intracranial lesions resulting in primary non-expansion of the lungs; (*c*) intracranial lesions allowing expansion of the lungs initially; (*d*) primary lung lesions; and (*e*) congenital cardiac lesions. It was found that respiratory difficulties of cerebral origin could be distinguished from those of pulmonary origin by the rela-

tively slight degree of atelectasis present although respiratory distress was severe. Miliary mottling, localized or diffuse, suggested hyaline membrane, but could be simulated by pneumonia or haemorrhagic disease affecting the lungs. The author uses the term "diffuse primary alveolar atelectasis" for a condition in which respiratory distress is due to a failure of the alveoli to expand, when radiologically the lungs show a diffuse ground-glass appearance. *David Morris*

1041. **A Study of the Uptake of Iodine (I^{131}) by the Thyroid of Premature Infants**
E. E. MARTMER, K. E. CORRIGAN, H. P. CHARBENEAU, and A. SOSIN. *Pediatrics* [*Pediatrics*] **17**, 503–509, April, 1956. 1 fig.

1042. **Mental Ability and School Achievement of Premature Children at 8 Years of Age**
J. W. B. DOUGLAS. *British Medical Journal* [*Brit. med. J.*] , 1210–1214, May 26, 1956. 3 figs., 10 refs.

In the study here reported from the University of Edinburgh of the growth and development of a national sample of premature children born in March, 1946, the author presents the results of reading, vocabulary, and picture intelligence tests carried out on 676 of the children at 8 years of age, these being compared with the results in a similar number of control children born at term and matched for family position, mother's age, social group, and degree of crowding in the home, and whenever possible from the same administrative area.

In each of the tests the premature children were slightly but significantly more handicapped than the controls, this being more apparent in the reading test than in the vocabulary or picture intelligence tests. To ascertain the role of environmental factors other than economic (for example, special parental care) pairs were grouped by the occupation of the father; this revealed no difference in the reading test but the handicap for the vocabulary and picture intelligence tests was less in the children of non-manual workers. Analysis of the degree of handicap according to birth weight or duration of gestation revealed no significant correlation. A surprising finding was that premature infants born of uncomplicated pregnancy showed greater handicap than those born of pregnancies in which there was a history of toxaemia, antepartum haemorrhage, or induction of labour. In the search for a possible genetic factor premature children in whom there was no known obstetric reason for prematurity were compared with full-term children in three groups: those whose mothers were (1) smaller *and* lighter, (2) smaller *or* lighter, and (3) both taller and heavier than the mother of the matched control. The handicap was found to be smallest in the premature children in Group 1, in which there was the strongest evidence of a genetic element to account for the low birth weight; conversely, it was greatest in Group 3, in which there was least evidence of such a genetic element. As the author points out, these findings need confirmation, preferably by a more intimate and detailed study, and if confirmed, some explanation of their significance. *David Morris*

CLINICAL PAEDIATRICS

1043. **Some Observations on Headache and Eye Pain in a Group of Schoolchildren**
E. L. HUGHES and C. E. COOPER. *British Medical Journal* [*Brit. med. J.*] **1**, 1138–1141, May 19, 1956. 12 refs.

The authors discuss 85 out of 189 cases of headache and eye pain which could be related to tender areas in the posterior muscles of the neck; they occurred among school-children in the county of Northumberland who were specially referred to the school doctor by their teachers or parents because of the complaint. In 47 cases the headache or eye pain could be reproduced by pressure over the tip of one or both transverse processes of the first cervical vertebra, while in a further 38 cases the tip was very tender but the pain could not be reproduced on pressure. In many cases there was faulty posture, especially during reading or at the cinema, while in others there seemed to be a relationship to anxiety. In a few children the pain cleared up spontaneously; in the majority of the others it responded to simple explanation and relaxation exercises, and the tenderness over the tip of the first transverse process also disappeared.

As a guide to the incidence of the condition the authors report that of 3,811 children examined, 361 (10·2%) complained of headache, severe in 43 cases and mild in 318; the highest incidence (17·5%) was among the 10-year-olds. The nature of the lesion is not known, nor is the mechanism by which a lesion in the basi-occipital region can cause pain to be referred to the orbit or frontal area of the head. *Marianna Clark*

1044. **A Study of the Association of Prenatal and Paranatal Factors with the Development of Tics in Children. A Preliminary Investigation**
B. PASAMANICK and A. KAWI. *Journal of Pediatrics* [*J. Pediat.*] **48**, 596–601, May, 1956. 10 refs.

1045. **The Treatment of Congenital Myxoedema with DL-3:5:3′-Triiodothyronine.** (Le traitement du myxoedème congénital par la DL-3:5:3′-triiodothyronine)
M. LELONG, R. JOSEPH, P. CANLORBE, G. DELTOUR, P. BORNICHE, and R. SCHOLLER. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **32**, 1777–1780, May 22, 1956. 11 refs.

The authors report from the Hôpital Saint-Vincent-de-Paul, Paris, the results of the treatment of 6 cases of cretinism with DL-3:5:3′-triiodothyronine, which is considered to be one of the most active constituents of the thyroid hormone. At the beginning of treatment 4 of the children were under, and 2 were over, one year of age; 3 of them had previously been treated with thyroid extract. All 6 patients presented the characteristic appearances and signs of cretinism, together with clinical and radiological evidence of delay in skeletal maturation. Radioactive-iodine studies showed diminished thyroid uptake in 3 cases and normal uptake in the other 3. The latter 3 patients were consequently considered to

* Correction — p. 485
It was implied as a result of an editorial error that the study of the growth & development of premature children reported by Dr. J. W. B. Douglas ... was carried at at Univ. of Edinburgh, where author now held appt. In fact this work was part of a survey which is being made by a joint committee of the Population Investigation Committee, Society of Med. Officers of Health, & the Governors of Hosp. for Sick Children, with support of Nuffield Foundation, board member of regional boards. Great Ormond Street, Ford Foundation, & a

be suffering from "myxoedema through metabolic defect" and are being studied further.

The dose of triiodothyronine varied from 0·1 to 0·3 μg. per kg. body weight per day (stated by the authors to amount to 25 to 100 μg. daily). There were no toxic side-effects except in one child aged 3 receiving a dose of 50 μg. per day who developed an irregular pyrexia without other signs. The pyrexia ceased when the dose was temporarily reduced to 25 μg. per day. The external appearance of the children became normal within 6 weeks to 3 months after the institution of therapy, the gain in height was between 10 and 15% annually, and skeletal maturation was accelerated. However, mental development became normal in one child only, in whom treatment was begun at the age of 7 months.

The authors conclude that these results are qualitatively comparable with, but are not superior to, those obtainable with thyroid extract. In particular the skeletal underdevelopment does not appear to improve any more quickly. On the other hand triiodothyronine can be more exactly standardized than can thyroid extract, and a much smaller dose can be given. *Marcel Malden*

1046. **Metabolic Studies on Two Infants with Idiopathic Hypercalcaemia**

H. G. MORGAN, R. G. MITCHELL, J. M. STOWERS, and J. THOMSON. *Lancet* [*Lancet*] **1**, 925–931, June 16, 1956. 3 figs., 48 refs.

The authors report, from St. Andrews University, the detailed clinical and biochemical findings in 2 infants treated at Dundee Royal Infirmary for idiopathic hypercalcaemia. Balance studies showed that there was excessive absorption of calcium and phosphorus (up to 60%) resulting in hypercalcaemia, despite a high urinary calcium excretion. The oral administration of cortisone greatly increased the faecal excretion of calcium and phosphorus and reduced the plasma levels of these elements with consequent marked improvement in the clinical condition. Administration of disodium ethylenediaminetetracetic acid (EDTA), a chelating agent, appeared to lower the plasma calcium level, but proved too toxic for clinical use. A satisfactory low-calcium diet was eventually established and in one case led to gradual clinical improvement.

The high intestinal calcium absorption in such cases is considered to be due to the overaction of vitamin D, either arising from overdosage or because of the patient's hypersensitivity to the vitamin. One of the infants died; the blood urea level was high and at necropsy gross foci of calcification were found in the renal medulla; renal damage is the greatest danger of the condition. Discussing 15 cases of hypercalcaemia seen at Dundee in the course of 2 years, the authors state that in every case a supplement of vitamin D was being taken. They point out that in an infant given dried milk and later cereal, both fortified with vitamin D, as well as cod-liver oil the daily intake of the vitamin "may easily exceed 2,000 i.u.". They recommend treatment with a low-calcium diet and the oral administration of cortisone as necessary when rapid reduction of the plasma calcium level is required. *Winston Turner*

1047. **The Natural History of Pulmonary Collapse in Childhood**

U. JAMES, F. S. W. BRIMBLECOMBE, and J. W. WELLS. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **25**, 121–136, Jan., 1956. 8 figs., 28 refs.

In an attempt to obtain an over-all view of the problem of pulmonary collapse in childhood, as diagnosed radiologically, to assess the importance of the various aetiological factors, and to review the course and prognosis of the disease the authors examined all the chest radiographs taken at the Princess Louise (Kensington) Hospital for Children, London, in the years 1945–52. Out of a total of nearly 5,000 children attending all departments of the hospital, 854 were accepted by all three authors as having radiological evidence of collapse —that is, of diminution in the size of one or more bronchopulmonary segments (the lingula being regarded as a functionally separate lobe), being present in a minority only. Of these, 472 attended a follow-up clinic for re-examination.

The 854 patients were divided into ten groups according to the aetiological factor involved, cases due to pertussis (18·9%), measles (3·6%), asthma (6·3%), tuberculosis (6·1%), and anaesthesia (2·3%) being easily distinguished, while those due to sinobronchitis (13·8%), upper respiratory infection (17·1%), lower respiratory infection (13·6%), and pneumonia (18·7%) were harder to differentiate. A miscellaneous group (3·4%) included 8 cases of pleural effusion with pneumonia and 9 cases of fibrocystic disease, all fatal; 9 of the 29 patients in this group attended for follow-up examination and in none was there "persistent" collapse (that is, collapse of over 2 years' duration). The diagnosis of sinobronchitis was based on the presence of a long-standing, persistent, purulent nasal discharge, bronchitis, and low grade fever, with radiographs showing antral opacity in most cases. [It would appear that antral opacity was discounted in the absence of nasal discharge.] Persistent collapse was found in 16 (20%) of the 80 patients in this group who attended the follow-up clinic. Cases of upper respiratory infection included 115 of acute nasal catarrh and 39 of acute tonsillitis; persistent collapse was found in 3 out of 20 of the latter group and in one out of 62 of the former. Of 38 cases of collapse following lower respiratory infection (without acute respiratory distress or signs of consolidation) examined at follow-up, 3 were persistent, but none was bronchiectatic, and of 67 cases following pneumonia, again 3 showed persistent collapse, none with bronchiectasis. The cases in which collapse followed a typical history of pertussis showed a higher incidence of collapse of the right middle lobe and lingula than in previously reported series, possibly reflecting a more careful study of lateral views. Of 105 cases re-examined, collapse was persistent in 5, 2 with bronchiectasis; in 5 cases the lung had expanded only after one to 2 years. Measles tended to cause multilobar collapse, which was persistent in 2 out of 18 cases followed up, with bronchiectasis in both. Collapse was recurrent in at least 25% of cases of asthma and was persistent in 3 of 32 followed up, none with bronchiectasis. In 14 of 28 cases of tuberculosis followed up the collapse was persistent; the incidence of bronchiectasis could not be

accurately determined, but appeared to be high. Post-operative collapse occurred in 20 cases, the lung re-expanding in less than 21 days in 19 of them, with no persistence.

An analysis is presented in tabular form showing the different lobes affected, age, incidence, and recurrence rate in the ten groups. No special lobar pattern was found in cases where obstruction was thought to be due to aspiration or to secretions in the bronchial tree, but with obstruction from enlarged hilar lymph nodes the right middle and upper lobes were most commonly affected. In 58% of cases following pertussis the right middle lobe was collapsed, a higher incidence than has been reported in other series, probably reflecting a more careful study of lateral views; it is suggested that collapse was initiated by enlarged lymph nodes and later maintained by excess secretion. No case resembling the "middle-lobe syndrome" was found. Of 27 patients with collapse of more than 3 years' duration, 16 were free from symptoms and 8 were tuberculous, the right middle lobe being collapsed in only one of these. Isolated lobar collapse was most common in asthma and tuberculosis, in which the right middle lobe was most often affected. In other respiratory infections the left lower lobe was more liable to collapse.

Recurrent collapse was seen mainly in cases of sinobronchitis and asthma. The duration of collapse was less than 3 months in 240 of the 472 cases followed up, being longest in cases associated with sinobronchitis, pertussis, asthma, and tuberculosis. In 14 cases re-expansion occurred after one to 2 years and in 3 after 2 years. There were 50 cases of persistent collapse among those followed up, sinobronchitis (16) and tuberculosis (14) predominating as aetiological factors. Bronchography was carried out in only 24 of these cases, and showed bronchiectasis in 8.

[This paper represents much work, and the figures given will be quoted widely. The authors have been fortunate in finding no cases of mixed aetiology, such as asthma in a case of tuberculosis or bronchiectasis. Although it is not stated positively, it would appear that the duration of collapse in each case has been dated from the time of the first radiograph rather than from the onset of respiratory symptoms, and that the lungs were assumed to have been normal until then. It is worthy of comment that in a children's hospital during 7 years no single case presented as bronchiectasis with pulmonary collapse.] *A. White Franklin*

1048. **Staphylococcal Pneumonia in Infants**

M. E. DISNEY, J. WOLFF, and B. S. B. WOOD. *Lancet* [*Lancet*] **1**, 767–771, May 26, 1956. 2 figs., 20 refs.

Of 530 infants under the age of 2 years admitted to Dudley Road Hospital, Birmingham, in 1953 and 1954 with infections of the lower respiratory tract 35 had staphylococcal pneumonia. (In 6 cases, which are not further discussed, the condition was secondary to serious underlying disease—for example, fibrocystic disease of the pancreas.) Diagnosis was established on the basis of the clinical features and radiological signs of pneumonia and pneumatocele formation. Culture of laryngeal, post-nasal, and throat swabs from 19 infants revealed *Staphylococcus aureus* in only 5. Of 25 infants subjected to thoracic puncture, 8 had pleural effusion, all the specimens yielding *Staph. aureus*. In the remaining 17 cases there was no visible exudate in the syringe, and the needle was therefore inserted into glucose–broth, which was drawn up into the syringe and discharged back into the bottle for incubation. *Staph. aureus* was cultured in 14 of these 17 instances at the first attempt; in the remaining 3 the results of the initial lung puncture were negative and thus misleading.

All strains of *Staph. aureus* isolated were sensitive to erythromycin, all but one to chloramphenicol, and all except 2 strains to aureomycin and oxytetracycline. Erythromycin was used in treatment in 17 cases, but it did not appear to be superior to other antibiotics. It is now the authors' practice to keep erythromycin in reserve for cases showing bacterial resistance to all the other antibiotics. The results were considered to be satisfactory in that 25 infants recovered, while of the 4 who died, 3 succumbed within a few hours of admission —that is, before treatment could have become effective. In about half the infants, however, the pneumonia ran a relapsing course, which in retrospect seemed to be the result of too short a period of antibiotic treatment; the authors now recommend at least 21 days' treatment. There were no direct sequelae of thoracic puncture, although in one infant pyopneumothorax developed 8 days later; this however, was regarded as a complication of the staphylococcal pneumonia rather than of the puncture. The authors do not recommend lung puncture as a routine diagnostic procedure, but they state that by using it they have become more familiar with the early signs of staphylococcal pneumonia in infants.

K. C. Robinson

1049. **Non-specific Mesenteric Adenitis**

M. J. T. FITZGERALD. *Irish Journal of Medical Science* [*Irish J. med. Sci.*] 205–228, No. 365, May, 1956. 6 figs., bibliography.

Over a 12-month period, first at St. Kevin's Hospital, Dublin, and later at Oldchurch Hospital, Romford, the author made a special study of cases of non-specific mesenteric adenitis. The total number of patients of all ages admitted to these two hospitals during the period was 9,495; in 109 (0·87%) of these mesenteric adenitis was diagnosed, 99 of the affected patients being 5 to 20 years of age. From the study of these cases the author concludes that non-specific mesenteric adenitis is a clinical entity which, in the majority of cases, can be diagnosed at the bedside with some confidence. Since there is no laboratory aid to diagnosis reliance is placed on the typical history, signs, and symptoms. Haemolytic streptococcal infection appears to play no part in the aetiology of the condition, but upper respiratory tract infection is a significant predisposing factor. Circumstantial evidence suggests that a virus is the causative agent. Although the condition is self-limiting, the author considers that in cases in which the differential diagnosis is from acute appendicitis operation should be performed. *I. A. B. Cathie*

Public Health

1050. **Evaluation of the Quality of Work in Rural Hospitals on the Basis of Mortality.** (Оценка качества работы сельских больниц по показателям летальности)
I. E. GOLOVCHINER. *Советское Здравоохранение* [*Sovetsk. Zdravookh.*] 37–41, No. 3, May–June, 1956.

An analysis of the causes of death of patients in rural district hospitals in the Leningrad area [no actual rates are given] showed that pneumonia was responsible for 13·3% of all deaths, malignant disease for 12·4%, tuberculosis for 10·4%, trauma 10·1%, cardiac conditions 8·7%, hypertension 5·7%, and "dysentery" for 5·6%. When analysed by age groups the mortality distribution was as follows: patients under one year of age, 19·4%; one to 10 years, 12·4%; 11 to 25 years, 10·0%; 26 to 40 years, 10·1%; 40 to 55 years, 19·8%; and over 55, 27·9%. No very important conclusions are drawn on the work of these small hospitals. *R. Crawford*

1051. **Basic Problems of the Aged and Chronic Sick: Report of a Survey in Croydon, England**
T. H. HOWELL. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] 4, 224–234, March, 1956.

This paper presents an analysis of the medical and social problems of 509 elderly patients awaiting admission to Queen's Hospital, Croydon, a hospital for the chronically sick, who were interviewed. It was shown that admission was required for social as well as medical reasons in the majority (90%) of cases, and frequently delayed discharge. Of the medical reasons for admission and delayed discharge, degenerative lesions of the brain formed by far the largest group.

P. D. Bedford

1052. **Surface Film on Swimming Pools**
C. R. AMIES. *Canadian Journal of Public Health* [*Canad. J. publ. Hlth*] 47, 93–103, March, 1956. 1 fig., 27 refs.

Many different bacteria may be found in the water of public swimming-baths, but most of the recommended methods of analysis for routine use examine mainly for the presence of *Escherichia coli*. Writing from the Provincial Laboratory of Public Health, Edmonton, Alberta, the author points out that large numbers of organisms, bound up with mucus, from the nasopharynx and skin of bathers are found in the surface film on the water in swimming pools and that these organisms may be present when the deeper water, from which samples are usually taken, is free from *E. coli* because of the presence of chlorine. He suggests that the surface film should be given much more attention in bacteriological studies carried out by public health authorities, and describes a simple method whereby samples of this film to a depth of 0·5 mm. can readily be taken on pieces of calcium alginate gauze for subsequent culture. The organisms found in an investigation of the surface film from three bathing pools in Edmonton are reported. The author further recommends that the film should be frequently removed from the pool by a simple sweeping device, and that at times when there are many bathers the surface water (and film) should be allowed to escape down overflow gutters, which should not be placed only at the deep end. *Scott Thomson*

1053. **Antibody Responses to Naturally Occurring Poliomyelitis Infections. 3. Study of Household Contacts by the *p*H Indicator Method**
C. A. MILLER and M. F. LENAHAN. *Pediatrics* [*Pediatrics*] 17, 489–502, April, 1956. 4 figs., 12 refs.

Using the colorimetric metabolic-inhibition test of Salk *et al.* (*Amer. J. Hyg.*, 1954, **60**, 214; *Abstracts of World Medicine*, 1955, **17**, 255) the authors studied the neutralizing antibody response in 52 asymptomatic household contacts of patients with poliomyelitis, of whom 27 were faecal carriers of the virus and 25 had no virus in the faeces or symptoms. For purposes of comparison the antibody response in 25 patients with paralytic poliomyelitis who were all faecal virus carriers were also studied. Duplicate estimations were made on 51 of the serum samples in order to determine the degree of error of the technique. These showed that there was close agreement between the two series of test results in regard to whether antibody was present in the serum or not, a different result being obtained in 6 to 8% of the sera according to the type of virus against which they were tested. Much less agreement was achieved on the actual antibody titres, identical results being obtained in only about 60% of the sera. The second test gave antibody titres which differed from those of the first test by as much as fourfold or more in 37% of cases, the error occurring equally in either direction. The authors point out, therefore, that in view of the limitations of the test, data on antibody responses must be interpreted with caution. Half of all the subjects studied showed an increase of fourfold or more in the antibody titres of paired sera. This is three to four times as many as would be expected by chance.

From the serological data alone it was not possible to distinguish the antibody response of asymptomatic carriers of poliomyelitis virus from that of patients with paralytic poliomyelitis, or to distinguish either of these from the response of persons with a known recent exposure to poliomyelitis virus, but who neither showed symptoms nor were faecal carriers of the virus. Paralysed patients, however, exhibited antibody titres of 1 in 256 or more with rather greater frequency. The administration of gamma globulin to 25 persons within the 2 weeks before the first serum specimen was taken did not interfere either with the final level of antibody or with the demonstration of fourfold increase or more in the antibody titre. After repeated tests only one person was found who failed to develop homologous antibody to the virus carried in the faeces.

[All the test results are given in full detail in tables and diagrams, for which the original paper should be consulted.] *John Lorber*

1054. **A Continuous Study of the Acquisition of Natural Immunity to Poliomyelitis in Representative Louisiana Households**

J. P. Fox, H. M. Gelfand, D. R. LeBlanc, and D. P. Conwell. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **46**, 283–294, March, 1956. 2 figs., 22 refs.

The authors present, from Tulane University of Louisiana, New Orleans, an interim report (as part of a 5-year survey which was begun in 1953) on some 150 representative households in Louisiana which were observed for evidence of poliomyelitis infection, the households selected being those to which a child, the "index child", had recently been born. They were situated in one semi-rural and two urban districts, and in each district the proportion of white to negro households and the family size were roughly similar. Specimens of blood and faeces were collected monthly from the index child, and blood specimens annually from other members of the household. Virus isolations were made from the faeces using HeLa-cell tissue-cultures, which were later abandoned in favour of tissue cultures of monkey kidney. Neutralization tests were performed on the blood samples, using an initial serum dilution of 1 in 2 (final) and employing 100 tissue-culture doses of each of the 3 serological types of poliomyelitis virus. Whenever evidence of poliomyelitis infection was found another visit was made to the household to determine how far the infection had spread.

The results reported are those in respect of the period April, 1953, to September, 1955, during which time no case of paralytic poliomyelitis was recorded in either the index children or their household contacts. Nevertheless 109 index children showed evidence, either by isolation of the virus or by serological response, that they had been infected with the virus of poliomyelitis during that period. Although 15 of the infections occurred during the first 7 months of life, only 4 were shown to occur in the presence of persisting maternal antibody. While most of the infections took place during the late summer and early autumn, it was clearly shown that infections continued to take place, although at a lower rate, throughout the year. In 1954 there was a predominance of infections due to Type-3 virus, whereas in 1955 Type-1 infection predominated. During 1953–4 (the only period for which complete details were available) 82 out of 86 previously non-immune household contacts became infected by the index children. Examination of samples of faeces from 69 of these children showed that poliomyelitis virus was present in 34. Among 161 previously immune household contacts, 31 showed a fourfold or greater increase in neutralizing antibody titre, indicating that reinfection had occurred—but virus was isolated from the faeces on only one occasion. Individuals who showed evidence of reinfection tended to be those whose antibody titre before reinfection was low (median titre 1 in 40). A history of possibly significant symptoms of minor illness was obtained in about 36% of persons who were infected. If the age-specific infection rates observed in this survey are applied to the total population of the areas studied, it is calculated that for every notified case of paralytic poliomyelitis which occurred in 1954 there were 710 "silent" infections. *J. E. M. Whitehead*

1055. **Outbreak of Type 3 Poliomyelitis on St. Paul Island, Alaska**

C. M. Eklund and C. L. Larson. *American Journal of Hygiene* [*Amer. J. Hyg.*] **63**, 115–126, March, 1956. 12 refs.

The study of outbreaks of poliomyelitis in communities previously unexposed to the virus ("virgin soil" epidemics), provided adequate laboratory investigations are carried out, may afford useful information concerning the clinical and epidemiological manifestations of the different viral serotypes. The explosive outbreak described here, which occurred among the 322 Aleutian inhabitants of St. Paul Island (Pribiloff Group), Alaska, is the first recorded outbreak of this nature due to Type-3 poliomyelitis virus, and the behaviour of the virus contrasts markedly with earlier accounts of outbreaks due to Type-1 strains. The infection was most probably imported from the mainland by a 5-year-old child in the middle of winter (December 17, 1953), and was rapidly disseminated among the other children on St. Paul. In all, 32 cases of illness resulted, 27 of them being in persons under 17 years old and most of them occurring within a 2-week period. No cases of spinal paralysis occurred, the clinical forms being either bulbar, meningeal, or a minor febrile illness.

Poliomyelitis virus Type 3 was isolated from the faeces of 58 out of 76 persons under 17 years of age. A serological survey carried out 9 months after the outbreak showed that neutralizing antibodies to Type-3 virus were present in 99 out of 102 persons under 20 years of age and in 24 out of 37 over that age. No antibodies against Type-1 virus were found, and antibodies against Type-2 virus were present only in persons aged 33 or more. No recognizable cases of poliomyelitis had previously occurred in this community, whose living standard was similar to that of "the laboring class in a community in the northern United States". Reasons are given for considering that the mode of spread of the infection was from person to person. *J. E. M. Whitehead*

1056. **Respiratory Virus Infections in R.A.F., 1954–5**

B. E. Andrews, J. C. McDonald, W. B. Thorburn, and J. S. Wilson. *British Medical Journal* [*Brit. med. J.*] **1**, 1203–1207, May 26, 1956. 2 figs., 15 refs.

To determine the prevalence of infections with the A.P.C. group of viruses and others and to study the relation between circulating antibody levels and susceptibility to influenza a survey was made of respiratory illness at 10 R.A.F. stations during the 4 months December, 1954, to March, 1955. None was a recruit station. Blood was taken from 1,001 healthy volunteers at the beginning, and from 711 of them again at the end of the period, while throat washings and paired blood specimens were obtained from a number of patients during outbreaks of

respiratory infection at 6 of the stations. Complement-fixation tests for influenza A, B, and C and the A.P.C. virus group were performed with soluble antigens, the A.P.C. antigen being prepared from HeLa-cell cultures infected with the RI-67 strain.

The average admission rate for respiratory illness was 6·9% of the total strength and for the 711 volunteers from whom two specimens of blood were obtained the rate was 5·6%. There was serological evidence of infection with influenza B in 19%, with influenza A in 1%, and with A.P.C. virus in 0·03% of the volunteers. A fourfold rise in the titre of antibody to *Streptococcus* M.G. occurred in 2%. There was no evidence of infection with the psittacosis–L.G.V. group of viruses or *Rickettsia burneti*.

The antibody titres against influenza B of 26 volunteers who developed respiratory infections at 5 stations which had outbreaks of influenza B were compared with those of 78 volunteers who were not infected. An initial titre of 1:2 or more was more frequently found among the latter, and a fourfold rise in titre during the period of the study in the former.

At one station an outbreak of respiratory illness occurred in mid-March, 1955. Throat washings were taken from 7 patients during the first 3 days of illness and 5 yielded viruses of the A.P.C. group, while 7 out of 24 paired sera showed a rise in the titre of antibody to RI-67, and 6 in that of influenza A antibody. Out of 45 convalescent sera, in 15 the A.P.C. antibody titre was 1:10 or more. The symptoms and signs of this illness were similar to those of influenza. *G. C. R. Morris*

1057. **Active Immunization with Influenza Virus A and B in Infants and Children**

M. M. Glazier, A. S. Benenson, and R. E. Wheeler. *Pediatrics* [*Pediatrics*] **17**, 482–488, April, 1956. 11 refs.

Between 1946 and 1953 614 children aged 4 months to 16 years (median 2·7 years) were inoculated with one of two types of commercially prepared influenza-A and -B vaccine which were claimed to have a high degree of purity, stability, antigenicity, ease of standardization, and uniformity among different lots; 577 of the patients received a second dose one week later and 321 a booster dose about 3 months later. All the patients showed moderate local reactions for up to 10 days. One-quarter of the children had systemic reactions, which were far commoner after the initial injection than after the booster dose. The reaction included fever, malaise, headache, rigor, abdominal pain, vomiting, and diarrhoea, in that order of frequency. Reactions were commoner in those given the higher dosages, but were not related to a family or personal history of allergy; they were severe in 9·2% of the patients.

The serological response was estimated in 63 children and was considered good, even in those who received the smallest doses. The booster doses resulted in a further considerable increase in antibody titre to influenza A and B virus, which persisted above the pre-immunization level for 12 to 18 months. The authors believe that the results suggest that primary inoculation is fairly effective with a single injection of 0·1 ml. given intradermally or 0·2 ml. subcutaneously, but better and more rapid response in antibody titre is likely when two injections each of 0·1 ml. are given a week apart. Larger doses do not produce a higher titre. A small booster dose of 0·1 ml. was as effective in producing a further rise in antibody as a large one (1 ml.).

The advisability of immunization is discussed. It is felt that although such immunization is not likely to protect against all influenza epidemics and although toxic reactions are fairly frequent, they may serve a useful purpose since they have been reported to reduce to one-quarter the number of clinical attacks.

[The authors make no reference to clinical results, nor were any antibody levels studied in comparable control subjects who had not received anti-influenza inoculations. Moreover, the number of children on whom antibody levels were determined was very small in comparison with the total number immunized.] *John Lorber*

1058. **A Second Outbreak of Boston Exanthem Disease in Pittsburgh during 1954**

F. A. Neva. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 838–843, May 3, 1956. 1 fig., 3 refs.

The author gives an account of an outbreak, in June, 1954, of a disease which was characterized by several days of fever and a rash lasting one to 3 days and appeared on clinical evidence to be communicable, with an incubation period of 3 to 7 days. The outbreak affected a small suburban community of about 31 homes some 8 miles from the centre of Pittsburgh which was partially isolated from adjacent residential areas. There was generally free and unrestricted association between the children of the households, but there was no "crowding" of the houses, which accommodated 60 adults (mostly under the age of 50) and 46 children (mostly under the age of 10). Within this community 17 cases were diagnosed clinically and in 13 of these the diagnosis was subsequently confirmed by the isolation from the faeces, throat, or blood of a virus with a constant cytopathogenic effect in tissue-cultures or by the demonstration in the serum of a rising titre of neutralizing antibodies against this virus. These cases all occurred within a 12-day period and affected 10 of the 31 households; there were 4 cases of multiple illnesses within a single household, 3 involving an adult as well as children. The ages of the 11 children affected varied from 5 months to 9 years, and those of the 6 adults from 28 to 35 years. Three additional cases were suspected on the basis of the clinical history but were not further investigated.

The same disease was suspected, on both clinical and laboratory evidence, in 7 other cases which occurred sporadically in 4 widely separated households in the city itself during the subsequent months of July, August, and September. In only one case was there a possible association with the suburban outbreak.

A short description is given of 4 suburban and 2 of the later cases. The clinical, laboratory, and epidemiological findings are said to have been practically identical with those in a similar outbreak in Boston in 1951 involving 13 children and 2 adults. *J. Cauchi*

Industrial Medicine

1059. **Silo-filler's Disease**

L. T. Delaney, H. W. Schmidt, and C. F. Stroebel. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **31**, 189–198, April 4, 1956. 3 figs., 3 refs.

In October, 1955, after a vague illness of 2 weeks' duration, a 43-year-old farmer became acutely ill with a high temperature, nausea, vague abdominal pains, anorexia, and chills, followed by cough and increasing dyspnoea. The clinical and radiographic manifestations were those of acute pneumonitis. Treatment at home and in hospital with a variety of antibiotics and general supportive therapy proved unavailing and the patient died on the fifth day of his illness. Post-mortem examination showed extensive congestion and oedema of all lobes of the lungs, which was confirmed histologically, but otherwise nothing significant. A month previously a 59-year-old farmer had been treated in the same hospital for a similar condition, but in this case the symptoms were less severe and the patient ultimately recovered. From a study of the histories of these cases it emerged that one factor was common to both, namely, that at the time of onset of the illness each had been engaged in filling silos with newly chopped corn silage. Enquiries produced reports of a number of cases of the same sort which had occurred in the district in similar circumstances. It had also been observed that the corn forage at the bottom of the silos and on the floor of the chute developed an unusual yellow or orange colour associated with the presence of a brownish gas, and there were scattered reports during the preceding 10 years that chickens, pigs, and cattle had died after exposure to this forage.

Analyses carried out at the College of Agriculture of the University of Wisconsin on air samples collected near the floor of a room communicating by a door with a recently filled silo revealed the presence of nitrogen dioxide (NO_2) in a concentration of 151 parts per million, which contrasts with a maximum allowable concentration in American factories of 25 parts per million. It was concluded that the gas was generated by the reduction of nitrates following fermentation in the corn. This reaction was assisted by poor ventilation and by high atmospheric temperatures. Fortunately the production of the gas stops within a few days and, so far as can be determined, there is no subsequent danger from the use of the silage. Reports of the clinical effects of inhalation of NO_2 from other sources are discussed in relation to the authors' cases and others which have come to their notice, and they conclude that there is a definite relationship between the pulmonary disease and silo-filling under closed conditions and in high temperatures. They suggest that this hazard and the condition resulting from it is more common than has hitherto been realized. They further state that " speculation as to any relationship between silo-fillers' disease and the syndrome of farmers' lung, as we have been familiar with it in later phases associated with pulmonary fibrosis, seems as yet unwarranted ".

The authors recognize that their conclusions are based on very limited experience, but [rightly] consider it advisable to report the hazard so that preventive measures can be adopted and further observations made.

A. Meiklejohn

1060. **Aluminium Powder Inhalations in the Treatment of Silicosis of Pottery Workers and Pneumoconiosis of Coalminers**

M. C. S. Kennedy. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **13**, 85–99, April, 1956. 13 figs., 29 refs.

A controlled trial of aluminium inhalations in the treatment of pottery workers' and coalworkers' pneumoconiosis has been carried out over 4 years. One hundred and twenty patients were selected to meet certain criteria and were then separated by pairing into 2 equal groups comparable as regards age, sex, industrial history, and the manifestations of the disease. The individuals were then randomly allocated to the 2 forms of treatment.

Group A received pure metallic aluminium dust and Group B pure carbon (powder) with the addition of 1 p.p.m. pure metallic aluminium powder. Both groups were given 15-minute inhalations 3 times each week for as long as $3\frac{1}{2}$ years (or for such less time as the patient continued in the trial).

All subjects were assessed before treatment and during the first, second, third, and fourth years of treatment, and were found to run a parallel course. A major proportion of both groups claimed symptomatic improvement, but the number was only slightly more than those claiming improvement after breathing (unknown to the patient) pure atmospheric air from the cabinets for six weeks. There was no regression of the radiological picture, nor was there objective evidence of improvement in the functional capacity of patients as judged from the results of the exercise tolerance test, the vital capacity, and the maximum voluntary ventilation.

Although there was symptomatic improvement of a general nature in both groups, it is concluded that this improvement was mainly psychological in origin and that the specific inhalation therapy did not produce either any regression in the established disease or an improvement of the patients' functional capacity.

There was no evidence that the aluminium inhalations favoured the development of pulmonary tuberculosis in patients with coalworkers' or pottery workers' pneumoconiosis.—[Author's summary.]

1061. **A Study of the Effects on the Lung of Industrial Exposure to Zirconium Dusts**

C. E. Reed. *A.M.A. Archives of Industrial Health* [*A.M.A. Arch. industr. Hlth*] **13**, 578–580, June, 1956. 1 fig., 3 refs.

Radiology

RADIODIAGNOSIS

1062. **A Clinical and Radiological Study of Choanal Polypi**

D. F. Reynolds and H. J. Groves. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol. (Lond.)*] **7**, 278–285, April, 1956. 11 figs., 3 refs.

In planning the treatment of a choanal polypus the surgeon must know from which side of the nose it is arising and whether it arises from the antrum. This is frequently not evident on clinical examination alone. Indeed, in difficult cases it may be impossible to see the polypus at all by rhinoscopic methods.

Radiographically choanal polypi can be reliably visualized in the lateral view of the nasopharynx. They can often also be suspected in the occipitomental view, where they may be projected below the symphysis menti. The side of origin is indicated by loss of the normal translucency on the affected side within the nasal cavity, and in the occipitomental view its shadow at the choana on one side is most convincingly shown through the mouth. When the polypus arises from a maxillary antrum, this shows either a uniform loss of translucency, or a soft-tissue mass largely filling the antrum. We have not found the appearance of simple mucosal thickening in antra from which choanal polypi arose. In the lateral view an air track usually separates the top of an antrochoanal polypus from the roof of the nasopharynx. When the polypus arises from sinuses other than the antrum the affected sinus (usually ethmoidal) shows loss of translucency. In most of these cases there is no air space between the polypus and the nasopharyngeal roof. The sinus of origin of the polypus is generally not the only one to show radiological abnormalities.

Care must be taken to distinguish choanal polypi from true neoplasms arising anteriorly and projecting backwards into the nasopharynx.—[Authors' summary.]

1063. **Radiology of the Lung in Left Heart Failure**

D. S. Short. *British Heart Journal* [*Brit. Heart J.*] **18**, 233–240, April, 1956. 5 figs., 20 refs.

The results of a study of the radiological appearances of the lung in 51 cases of left heart failure or left ventricular enlargement are reported from the London and the Middlesex Hospitals. The cases were consecutive except that patients in whom there was evidence of organic disease of the mitral valve or of the lung parenchyma were excluded; thus patients with emphysema were excluded, but not those with bronchitis alone. An abnormal lung pattern was noted in 67 radiographs from 39 patients, the commonest abnormality being hilar clouding. Involvement of the pleura, the next most frequent abnormality, was observed in 51 radiographs: hydrothorax was present in 29 instances and widening of the horizontal or oblique fissure in the remainder. Short horizontal lines were seen in the costophrenic angles in 20 radiographs and were associated with a small effusion in 10; they were similar to the lines encountered in severe mitral stenosis, although they were less numerous and less sharply defined. Enlargement of the pulmonary trunk was observed in 13 radiographs, and in one instance the enlargement extended into the main branches; the calibre of the intrapulmonary arteries was within normal limits. Pulmonary congestion was demonstrated in 7 patients in whom the existence of heart failure was uncertain clinically.

The author considers that radiology is most helpful in the diagnosis of left heart failure. He points out that failure of the left ventricle leads to a rise in pressure, primarily in the left atrium and secondarily in the pulmonary artery. In well-marked left failure right ventricular hypertrophy occurs and pulmonary hypertension may be as severe as in mitral stenosis. The difference between the pattern of pulmonary congestion in left heart failure and that in mitral stenosis is discussed.

Sydney J. Hinds

1064. **Bronchography with "Dionosil" ("Propyliodone")**

J. K. V. Willson, F. R. Perilla, and R. B. Hanchett. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **75**, 720–727, April, 1956. 5 figs., 10 refs.

Experience with "dionosil", a new contrast medium, in bronchography is reported from the Johns Hopkins and Veterans Administration Hospitals, Baltimore. Dionosil is chemically very similar to diodone, but is insoluble in water or body fluids; it is supplied as an aqueous suspension or an oily (arachis oil) suspension. Free iodine is not released, and the medium is absorbed completely from the lungs after hydrolysis and is excreted by the kidney in the course of a few days. Aqueous dionosil coats the bronchial mucosa but seldom floods the alveoli. This preparation is somewhat more irritating than oily dionosil, and British workers report that premedication with a morphine derivative is desirable and obviates coughing. No immediate reactions have been reported, but in some patients a transient rise in temperature and slight malaise were observed on the day after examination. Oily dionosil is less irritating and no reactions have been reported. With this preparation there is a greater tendency to alveolar filling. Clearing of the contrast medium is rapid, only traces of the oily base being seen in the alveoli a few days after bronchography.

The authors used dionosil for 50 consecutive bronchograms (48 cases), all of which were of excellent quality, 26 being obtained with the aqueous and 24 with the oily medium. The series included 14 cases of tuberculosis; in none of these did the procedure have any apparent

effect on the course of the disease. As expected, tuberculous cavities did not fill. One patient with moderately-advanced tuberculosis and one whose lungs were emphysematous experienced some shortness of breath immediately after bronchography with aqueous dionosil, but this was transient. Delayed reactions were of a minor character and were similar to those reported by workers in Britain. The authors conclude that for general use dionosil is preferable to iodized oil. *A. M. Rackow*

1065. **Routine Operative Cholangiography: a Critical Five Year Review**
G. M. Brown and B. H. Brown. *American Surgeon* [*Amer. Surg.*] **22**, 415–419, April, 1956. 2 refs.

The findings in 225 consecutive cases of biliary-tract surgery in which operative cholangiography was used are summarized in this paper from McAlester Clinic, Oklahoma. Needle cholangiography was abandoned in favour of catheter cholangiography, in which a polythene tube was placed in the cystic duct, and three injections, each of 3 ml. of 70% "urokon" sodium, were given, a cholangiogram being taken after each injection. If common-duct exploration was undertaken, terminal cholangiography was performed along the T tube before closure of the abdomen. The common duct was explored in 2 cases because of false positive cholangiograms. In 19 cases re-operation was avoided because: (1) stones were found at cholangiography in a normal duct in which no indication for common-duct exploration was present; (2) intraductal strictures caused by scarring were found and corrected; (3) intrahepatic stones were demonstrated and removed; (4) terminal cholangiograms revealed residual stones after common-duct exploration; and (5) terminal cholangiograms showed misplacement of the tube.

The authors have not detected any reaction from the procedure; moreover, in none of the cases was there evidence of the post cholecystectomy syndrome.
Sydney J. Hinds

1066. **Combined Intravenous Cholecystography and Pyelography**
N. H. Aldridge. *British Journal of Radiology* [*Brit. J. Radiol.*] **29**, 127–132, March, 1956. 6 figs., 6 refs.

In patients complaining of vague abdominal pain it is often difficult to determine whether it originates in the biliary or urinary tract, and in practice many of these patients have to undergo both pyelography and cholecystangiography. The author, working at the General Infirmary at Leeds, has explored the possibility of combining the two investigations in order to save time and expense. Experimental work showed that no incompatibility existed between "biligrafin" and diodone (or sodium acetrizoate) and that the toxicity of these media was not increased by mixing them. By virtue of the fact that the excretion of diodone or sodium acetrizoate by the kidneys is more rapid than the excretion of biligrafin by the liver, it was found possible, with a suitable technique, to visualize both systems separately after a single intravenous injection of the mixed media. Experience showed, however, that the shadow of sodium acetrizoate tended to persist longer than that of diodone and occasionally masked that of the gall-bladder.

The technique developed is as follows. After the usual preparation of the colon, a fatty meal is given to empty the gall-bladder. A control radiograph of the abdomen is taken 1½ hour later, followed by injection of the mixed contrast media (20 ml. of 20% biligrafin +20 ml. of 42·5% diodone). Ten minutes later a radiograph of the kidney region is taken, and if detail is satisfactory the patient is given 500 ml. of water to drink, the resulting diuresis so diluting the medium in the urinary tracts that its shadow does not interfere with the subsequent examination of the biliary tract. After another 5 minutes 25 to 50 mg. of pethidine is injected in order to close the sphincter of Oddi, and a second pyelogram and a cystogram taken. An oblique film of the gall-bladder area is taken approximately 30 minutes after the injection of the media and a second film, taken with the patient erect if necessary, is exposed 20 minutes later. If satisfactory filling of the gall-bladder and the ducts has been obtained, a second fatty meal is given, followed after 20 to 30 minutes by a further film.

In 50 cases examined by the author by this combined technique satisfactory visualization of both biliary and urinary tracts was obtained. In 10 cases in which the examinations were repeated separately the results with the combined technique were fully comparable with those of the separate investigations. There were no serious complications, and the usual side-effects associated with pyelography were no more frequent than when diodone is used alone.

The author emphasizes that this method is probably not suitable for routine use in a large department, but he claims that it is of value, for example, when rapid diagnosis is required or when repeated visits to hospital are impracticable. *R. Murray*

RADIOTHERAPY

1067. **Classification and Clinical Aspects of Acute Radiation Sickness in Man.** (Некоторые вопросы классификации и клиники острой лучевой болезни у человека)
Y. G. Grigor'ev. *Клиническая Медицина* [*Klin. Med.* (*Mosk.*)] **34**, 12–25, No. 3, March, 1956. 2 figs., 32 refs.

In this review of the clinical aspects of radiation sickness, which may be acute, subacute, or chronic, the author states that the acute form can be divided into four stages: (1) an initial period, (2) the period of temporary amelioration, (3) the critical period, and (4) the period of recovery. He then summarizes the findings of Gempel'man *et al.* who described in detail the results of the wrecking of a reactor, in which 9 persons were exposed to massive dosage of γ rays and soft x rays. The initial stage was manifested by prostration, nausea, vomiting, anorexia, hiccup, dyspnoea on exertion, hypotension, and diarrhoea; the blood picture showed granulocytosis, lymphopenia, thrombocytopenia, and acute cell destruction in the bone marrow. These

features continued throughout the second stage; in the third stage the general condition became worse, the patients suffering from blood-stained diarrhoea, tachycardia and arrhythmia, ulceration of the tongue, dryness of the throat and mouth, and widespread epilation. There was aplasia of the bone marrow, anaemia, and leucopenia. Two patients died at this stage, one on the 9th and the other on the 24th day. The remainder recovered after a slow convalescence extending over a period of 3 years. The hair began to grow again on the 45th day, and its growth was normal in 5 months. The patients were sterile for 28 months. Examination of the blood showed that the neutrophil leucocyte and thrombocyte count had returned to normal after 2 months, whereas the erythrocyte and lymphocyte counts recovered more slowly.

The course of the disease after the bombing of Hiroshima followed more or less the same course. Pyrexia was observed in 61% of cases, haemorrhage in 59%, epilation in 47%, ulceration of the throat in 23%, and gingivitis in 15%. Pneumonia, abscess of the lung, pleurisy, and pustulation of the skin were later complications; in the 6 years following the bombing, there were 53 cases of leukaemia among the 125,000 persons exposed to irradiation, that is, four times the normal morbidity of this disease. Cataract developed at intervals of from a few months to 3 years after the disaster; out of 1,313 people within a radius of one kilometre from the epicentre of the explosion, 109 cases of cataract were found in 1950.

Finally, the author describes the symptoms and outcome of therapeutic irradiation sickness in 136 patients. These, in order of frequency, were nausea, weakness, headache, drowsiness, vertigo, anorexia, vomiting, salivation, rigors, metallic taste in mouth, and olfactory hallucinations. The findings are compared with those reported by Brown (*Brit. med. J.*, 1953, **1**, 802; *Abstracts of World Medicine*, 1953, **14**, 438).

L. Firman-Edwards

1068. **The Role of Irradiation in the Treatment of Wilms' Tumor in Children**

H. D. KERR and R. E. FLYNN. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **75**, 971–976, May, 1956. 11 refs.

During the years 1931–51, 28 cases of Wilms's tumour were treated at the State University of Iowa Hospitals, with the following results. Of 14 patients treated by irradiation alone, 4 (28·6%) survived 2 years and 2 (14·3%) survived 5 years. Of 14 patients treated by irradiation and nephrectomy, 7 (50%) survived 2 years and 5 (35·7%) survived 5 years. It is concluded that although irradiation may hold the disease in abeyance, nephrectomy is essential for cure. One patient in the second group died after 64 months of " causes directly related to the irradiation of metastasis ", but no residual neoplasm was found at necropsy. Metastases appeared on average 42 months after nephrectomy with preoperative radiotherapy and 61 months after irradiation alone. A 2-year observation period is thus too short for the assessment of cure.

Radiation was delivered through opposing fields, a lateral field being added for large tumours, and was started as soon as the diagnosis was established, the tumour dose varying from 2,000 to 3,000 r. Nephrectomy was performed 8 to 12 weeks later. The patient was seen thereafter at 3-monthly intervals, and pulmonary metastases were treated with a tumour dose of 1,000 r to the region involved.

I. G. Williams

1069. **Combined X-ray and Radium Therapy for Carcinoma of the Urethra.** (Kombinierte Röntgen- und Radiumbehandlung bei Urethra-Carcinom)

S. HULTBERG. *Strahlentherapie* [*Strahlentherapie*] **99**, 171–184, 1956. 7 figs., 26 refs.

Carcinoma of the urethra is rare, and the prognosis has hitherto been very poor. A review by the author of all cases seen at Karolinska Sjukhuset, Stockholm, from 1918 to 1944 showed only one male and 6 female 5-year survivors out of 45. The earlier technique was to give intracavitary or interstitial radium combined with teleradium; this, however, did not give homogeneous dosage, often causing superficial necrosis with persistence of activity in the depths.

In 1945 a change was therefore made to *x*-ray therapy to give improved homogeneity, the factors usually being 170 kV, H.V.L. 1 mm. Cu, F.S.D. 50 cm., 4 vulval fields of 40 to 50 sq. cm. each, aiming at the posterior urethra, being employed. The dosage was 2,000 r to each field in 18 days, 500 r per day at skin level, giving 5,500 r at the orifice and 3,200 to 3,800 r at 4 cm. inside the urethra (as measured by a chamber in the canal). If a length of over 3 cm. of the urethra was involved, supplementary dosage was given by a vaginal box containing radium tubes filtered by 2 mm. lead equivalent; the box was loaded more heavily at the deep end, giving 4,000 r at 1 cm., and 1,500 r at 2 cm. depth in 20 hours.

Full details are given of 11 female patients treated between 1945 and 1951. Of these, 7 were symptom-free at 4 years, and 4 out of 9 survived at least 5 years. The treatment recommended for the various stages is as follows. For small superficial lesions, electrocoagulation with or without interstitial radium, or fractionated short-distance *x* rays; if the growth is 1 to 2 cm. in depth, deep *x* rays are given as above, or telegamma therapy; for more advanced growths, deep *x*-ray therapy, supplemented by intracavitary radium in the vagina or urethra; if the bladder is involved, radical cystectomy and postoperative external radiation are advocated. For inguinal-node metastases preoperative irradiation is advised, followed by radical surgery.

The incidence of carcinoma of the male urethra is too low to allow of any definite conclusion based on experience, but irradiation is considered unlikely to yield good results.

J. Walter

1070. **Preliminary Report on the Clinical Use of the Medical Research Council 8 MeV Linear Accelerator**

R. MORRISON, G. R. NEWBERY, and T. J. DEELEY. *British Journal of Radiology* [*Brit. J. Radiol.*] **29**, 177–186, April, 1956. 10 figs., 18 refs.